Journal of
THE CHEMICAL SOCIETY

Committee of Publication:

Chairman: Sir Cyril Hinshelwood, M.A., Sc.D., D.Sc., F.R.S.

Sir Wallace Akers, C.B.E., B.A., D.Sc., F.R.I.C.
R. P. Bell, M.A., B.Sc., F.R.S.
G. M. Bennett, C.B., M.A., Sc.D., F.R.S.
F. Bergel, D.Phil.Nat., D.Sc., F.R.I.C.
E. J. Bowen, M.A., D.Sc., F.R.S.
H. Burton, Ph.D., D.Sc., F.R.I.C.
A. H. Cook, Ph.D., D.Sc., F.R.I.C.
F. S. Dainton, M.A., Ph.D.
C. W. Davies, D.Sc., F.R.I.C.
M. G. Evans, D.Sc., F.R.S.
D. Ll. Hammick, M.A., D.Sc.
R. D. Haworth, D.Sc., Ph.D., F.R.S.
Sir Ian Heilbron, D.S.O., D.Sc., LL.D., F.R.S.
D. H. Hey, Ph.D., D.Sc., F.R.I.C.
A. King, C.B.E., D.Sc.
R. P. Linstead, C.B.E., M.A., D.Sc., F.R.S.
H. W. Melville, Ph.D., D.Sc., F.R.S.
L. N. Owen, Ph.D., D.Sc., F.R.I.C.
S. Peat, Ph.D., D.Sc., F.R.S.
S. G. P. Plant, D.Phil., M.A., B.Sc.
E. K. Rideal, M.B.E., M.A., D.Sc., F.R.S.
J. M. Robertson, M.A., D.Sc., F.R.S., F.R.I.C.
F. L. Rose, O.B.E., Ph.D., D.Sc., F.R.I.C.
H. N. Rydon, D.Sc., D.Phil., F.R.I.C.
C. W. Shoppee, D.Sc., D.Phil., F.R.I.C.
R. Spence, Ph.D., D.Sc., F.R.I.C.
D. W. G. Style, Ph.D.
S. Sugden, D.Sc., F.R.I.C., F.R.S.
A. R. Todd, M.A., D.Sc., F.R.S.
J. Walker, Ph.D., D.Phil., D.Sc.
W. Wardlaw, C.B.E., D.Sc., F.R.I.C.
T. S. Wheeler, Ph.D., D.Sc., F.R.I.C.
F. G. Young, M.A., D.Sc., F.R.S.

Editor:

R. S. Cahn, M.A., D.Phil.Nat., F.R.I.C.

Assistant Editors:

A. D. Mitchell, D.Sc., F.R.I.C.
L. C. Cross, Ph.D., A.R.C.S., F.R.I.C.

Indexer:

Margaret Le Fle, B.Sc.

OCTOBER, 1950

Subscription rate to non-Fellows £5 5s. 0d. *per annum post free.*

LONDON: THE CHEMICAL SOCIETY, BURLINGTON HOUSE, W.1

THE CHEMICAL SOCIETY

PATRON:
HIS MAJESTY THE KING

President:
E. K. RIDEAL, M.B.E., M.A., D.Sc., F.R.S.

Vice-Presidents
who have filled the office of President:

F. G. DONNAN, C.B.E., D.Sc., LL.D., F.R.S.
SIR IAN HEILBRON, D.S.O., D.Sc., LL.D., F.R.S.
SIR CYRIL HINSHELWOOD, M.A., Sc.D., F.R.S.
W. H. MILLS, M.A., Sc.D., F.R.S.
SIR ROBERT ROBINSON, O.M., D.Sc., LL.D., F.R.S.
N. V. SIDGWICK, C.B.E., D.Sc., LL.D., F.R.S.

Vice-Presidents:

R. P. BELL, M.A., B.Sc., F.R.S.
G. M. BENNETT, C.B., M.A., Sc.D., F.R.S.
J. W. COOK, D.Sc., F.R.I.C., F.R.S.
R. P. LINSTEAD, C.B.E., M.A., D.Sc., F.R.S.
A. R. TODD, M.A., D.Sc., F.R.S.
W. WARDLAW, C.B.E., D.Sc., F.R.I.C.

Treasurer:
SIR WALLACE AKERS, C.B.E., B.A., D.Sc., F.R.I.C.

Secretaries:

D. H. HEY, Ph.D., D.Sc., F.R.I.C.
A. KING, C.B.E., D.Sc.
H. BURTON, Ph.D., D.Sc., F.R.I.C.

Ordinary Members of Council:

J. S. ANDERSON, M.Sc., Ph.D., A.R.C.S.
G. BADDELEY, M.Sc., Ph.D.
C. E. H. BAWN, B.Sc., Ph.D.
L. L. BIRCUMSHAW, M.A., D.Sc.
G. R. CLEMO, D.Phil., D.Sc., F.R.S.
A. H. COOK, Ph.D., D.Sc., F.R.I.C.
F. S. DAINTON, M.A., Ph.D.
L. HUNTER, Ph.D., D.Sc., F.R.I.C.
F. E. KING, M.A., D.Phil., D.Sc.
T. MALKIN, Ph.D., D.Sc., F.R.I.C.
L. N. OWEN, Ph.D., D.Sc., F.R.I.C.
E. G. V. PERCIVAL, Ph.D., D.Sc., F.R.I.C.
J. D. ROSE, M.A., B.Sc.
R. SPENCE, Ph.D., D.Sc., F.R.I.C.
F. S. SPRING, Ph.D., D.Sc., F.R.I.C.
M. STACEY, Ph.D., D.Sc., F.R.S.
L. E. SUTTON, M.A., D.Phil., F.R.S.
A. I. VOGEL, D.Sc., D.I.C., F.R.I.C.
J. WALKER, Ph.D., D.Phil., D.Sc.
W. A. WATERS, M.A., Sc.D., F.R.I.C.
T. S. WHEELER, Ph.D., D.Sc., F.R.I.C.

Ex-Officio Members of Council:

H. E. COX, D.Sc., Ph.D., F.R.I.C. (*Chairman of the Joint Library Committee*).
A. FINDLAY, C.B.E., D.Sc., LL.D., F.R.I.C. (*Chairman of the Chemical Council*).
L. H. LAMPITT, D.Sc., F.R.I.C. (*Chairman of the Bureau of Abstracts*).

General Secretary:
J. R. RUCK KEENE, M.B.E., B.A.

Librarian:
A. E. CUMMINS.

Telephone Numbers: Regent 1675/6

THE CHEMICAL SOCIETY

SCIENTIFIC MEETINGS DURING NOVEMBER, 1950

LONDON.

Thursday, November 2nd, 1950.

Symposium, **Tropolones and Allied Compounds,** introduced by Professor J. W. Cook, D.Sc., F.R.S.

Afternoon Session at 2.30 *p.m.*

General Introduction. By J. W. Cook (Glasgow).
"Theoretical Considerations." By M. J. S. Dewar (Courtaulds, Ltd.).
"Thujaplicins." By H. Erdtman (Stockholm).
"Stipitatic, Puberulic, and Puberulonic Acids." By A. R. Todd and A. W. Johnson (Cambridge).
"Colchicine." By J. D. Loudon (Glasgow).

Evening Session at 7.30 *p.m.*

"Purpurogallin and some Degradation Products." By R. D. Haworth (Sheffield).
"Synthetic Tropolones—General Chemistry." By R. A. Raphael (Glasgow).
"Ultra-violet Absorption." By Mrs. G. Aulin-Erdtman (Stockholm).
"*X*-Ray Studies on Tropolone." By J. M. Robertson (Glasgow).
"The Infra-Red Spectrum of Tropolone." By H. P. Koch and W. Moffitt (British Rubber Producers' Research Association).

Abstracts of the papers for discussion may be obtained from the General Secretary.

Thursday, November 16th, 1950, *at* 7.30 *p.m.*

The following papers will be read and discussed:

"Macrozamin. Part II. The Presence of Linked Nitrogen Atoms in the Aglycone Part." By B. W. Langley, B. Lythgoe, and N. V. Riggs.
"Studies in the Organic Chemistry of Sulphur. Part II. The Alkaline Fission of some β-Aroyloxyethyl Dimethyl Sulphonium Iodides." By P. Mamalis and H. N. Rydon.
"An Experimental Study of Some Potentially Tautomeric 2- and 4(6-)Substituted Pyrimidines." By J. R. Marshall and J. Walker.

Abstracts of the papers may be obtained from the General Secretary.

ABERDEEN.

Wednesday, November 8th, 1950, *at* 5.30 *p.m.*

Lecture, **Some Aspects of the Chemistry of Polycyclic Aromatic Hydrocarbons,** by Professor J. W. Cook, D.Sc., F.R.S.

Joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, to be held in the Chemistry Department, Marischal College, Aberdeen. The lecture will be followed later in the evening by an informal dinner in the University Union.

BRISTOL.

Thursday, November 2nd, 1950, *at* 7 *p.m.*

Lecture, **The Hahn Emanation Technique,** by Dr. J. S. Anderson, M.Sc., A.R.C.S.

Joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, to be held in the Chemical Department of the University.

EDINBURGH.

Thursday, November 23rd, 1950, at 7.30 p.m.

Lecture, **Homolytic Aromatic Substitution,** by Professor D. H. Hey, D.Sc., F.R.I.C.

Joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, to be held at the North British Station Hotel.

EXETER.

Friday, November 10th, 1950, at 5 p.m.

Lecture, **Editing for the Chemical Society,** by Dr. R. S. Cahn, M.A., F.R.I.C.

To be given in the Washington Singer Laboratories, Prince of Wales Road, Exeter.

GLASGOW.

Friday, November 17th, 1950, at 7.15 p.m.

Lecture, **Some Problems in Gas Flow and Sorption,** by Professor R. M. Barrer, D.Sc., F.R.I.C.

To be given in the Chemistry Department, The University, Glasgow.

HULL.

Thursday, November 16th, 1950, at 6 p.m.

Lecture, **Recent Theories of Molecular Structure,** by Sir John Lennard-Jones, K.B.E., D.Sc., F.R.S.

Joint meeting with University College Scientific Society, to be held in the Science Lecture Theatre, University College, Hull.

LIVERPOOL.

Thursday, November 9th, 1950, at 4.30 p.m.

Lecture, **Polymerisation and its Reversal,** by Professor F. S. Dainton, M.A., Ph.D.

Joint meeting with the Royal Institute of Chemistry, the Society of Chemical Industry and the British Association of Chemists, to be held in the Chemistry Lecture Theatre, The University, Liverpool.

Thursday, November 23rd, 1950, at 4.30 p.m.

Lecture, **The Chemistry of Tropolone and some of its Derivatives,** by Professor R. D. Haworth, D.Sc., F.R.S.

Joint meeting with the Royal Institute of Chemistry, the Society of Chemical Industry and the British Association of Chemists, to be held in the Chemistry Lecture Theatre, The University, Liverpool.

MANCHESTER.

Wednesday, November 8th, 1950, at 6.30 p.m.

Lecture, **Catalysed Oxidation,** by Professor C. E. H. Bawn, Ph.D.

Joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, to be held in the Chemistry Department, The University, Manchester.

NEWCASTLE AND DURHAM.

Friday, November 10th, 1950, at 5 p.m.

Bedson Club Lecture, **Resonance Transfer of Energy between Molecules,** by Dr. E. J. Bowen, M.A., F.R.S.

To be given in the Chemistry Building, King's College, Newcastle-on-Tyne. All Fellows are invited.

Friday, November 24th, 1950, at 5 p.m.

Meeting for the Reading of Original Papers.

To be held in the Chemistry Building, King's College, Newcastle-on-Tyne.

NORTHERN IRELAND.

Tuesday, November 14th, 1950, at 7.30 p.m.

Lecture, **Some Problems in the Chemistry of the Polysaccharides,** by Professor E. L. Hirst, M.A., D.Sc., F.R.S.

Joint meeting with the Andrews Club, the Royal Institute of Chemistry and the Society of Chemical Industry, to be held in the Lecture Theatre, Department of Chemistry, Queen's University, Belfast.

Tuesday, November 28th, 1950, at 7.30 p.m.

Lecture, **Some Aspects of Cellulose Autoxidation,** by Dr. D. Entwhistle, A.R.I.C.

Joint meeting with the Andrews Club, the Royal Institute of Chemistry and the Society of Chemical Industry, to be held in the Lecture Theatre, Department of Chemistry, Queen's University, Belfast.

NORTH WALES.

Thursday, November 23rd, 1950, at 5.45 p.m.

Official Meeting. Tilden Lecture, **A Chemotherapeutic Search in Retrospect,** by Dr. F. L. Rose, O.B.E., F.R.I.C.

To be held in the Department of Chemistry, University College of North Wales, Bangor.

NOTTINGHAM.

Thursday, November 2nd, 1950, at 6.30 p.m.

Lecture, **The Cortisone Problem,** by Professor C. W. Shoppee, D.Sc., D.Phil., F.R.I.C.

Joint meeting with the University Chemical Society, to be held in the Chemistry Lecture Theatre, The University, Nottingham.

Thursday, November 9th, 1950, at 6.30 p.m.

Lecture, **Recent Chemical Applications of Electric Dipole Moment Measurements,** by Dr. L. E. Sutton, M.A., F.R.S.

Joint meeting with the University Chemical Society, to be held in the Chemistry Lecture Theatre, The University, Nottingham.

ST. ANDREWS AND DUNDEE.

Friday, November 3rd, 1950, at 5 p.m.

Lecture, **Chemical Aspects of the Cell Nucleus,** by Professor J. N. Davidson, D.Sc., M.D.

Joint meeting with the St. Andrews University Chemical Society, to be held in the Chemistry Department, United College, St. Andrews.

Friday, November 10th, 1950, at 5 p.m.

Lecture, **Bond Lengths, their Measurement and their Significance,** by Professor E. G. Cox, D.Sc., F.R.I.C.

Joint meeting with the Royal Institute of Chemistry, to be held in the Chemistry Department, United College, St. Andrews.

Friday, November 24th, 1950, at 5 p.m.

Lecture, **Homolytic Aromatic Substitution,** by Professor D. H. Hey, D.Sc., F.R.I.C.

Joint meeting with the St. Andrews University Chemical Society, to be held in the Chemistry Department, United College, St. Andrews.

SHEFFIELD.

Thursday, November 9th, 1950, at 6.30 p.m.

Lecture, **Hydrocarbons as Raw Materials for Organic Chemical Industry,** by Dr. R. J. Holroyd.

Joint meeting with the Royal Institute of Chemistry to be held in the Chemistry Lecture Theatre, The University, Sheffield.

Thursday, November 30th, 1950, at 5.30 p.m.

Lecture, **New Ventures in Carbohydrate Chemistry,** by Professor M. Stacey, D.Sc., F.R.S.

Joint meeting with the University Chemical Society, to be held in the Chemistry Lecture Theatre, The University, Sheffield.

SOUTHAMPTON.

Friday, November 17th, 1950, at 5 p.m.

Official Meeting. Lecture, **Kinetics of the Bacterial Cell,** by Sir Cyril Hinshelwood, M.A., Sc.D., F.R.S.

Joint meeting with Southampton University College Chemical Society, to be held in the Physics Department, University College, Southampton.

SOUTH WALES.

Friday, November 17th, 1950, at 5.30 p.m.

Lecture, **Ion Exchange Resins,** by Professor C. W. Davies, D.Sc., F.R.I.C.

Joint meeting with the Royal Institute of Chemistry and University College Swansea Chemical Society, to be held at University College, Swansea.

PROCEEDINGS

OF THE

CHEMICAL SOCIETY.

OFFICIAL ANNOUNCEMENTS.

DEATHS.

The Council regret to announce the deaths of the following Fellows:

	Elected.	Died.
Harold Adams (Wilmslow)	Sept. 5th, 1946.	Apr. 18th, 1950.
Donald Hugh Bangham (S.W.15)	Dec. 4th, 1919.	July 29th, 1950.
Harry Noel Griffiths (Manchester)	June 19th, 1941.	July 30th, 1950.
Oscar Watson Jarvis (S.W.11)	May 2nd, 1946.	Aug. 21st, 1950.
John Scott Lumsden (Dundee)	Mar. 6th, 1890.	July 12th, 1950.
Ernest Tom Neathercoat (Horsham) ...	Feb. 21st, 1924.	July 28th, 1950.
Theodore Rendle (Histon)	May 15th, 1941.	July 29th, 1950.
Henry Tigerman (Oklahoma)	Aug. 21st, 1947.	July 29th, 1950.
Thomas Richard Walker (Sheffield) ...	May 15th, 1941.	July 26th, 1950.

ELECTION OF NEW FELLOWS.

The following 51 candidates were elected Fellows of the Society on August 28th, 1950:

Norman Ashelford.
Evelyn Thomas Edward Barrow.
John Neville Baxter.
Gerald Andrew Bottomley.
Gerald Bulmer.
Michael Lyle Burstall.
Kenneth John Campbell.
Denis Coleman.
Frank William Donovon.
Gertrude Belle Elion.
Elvira A. Falco.
Bruce Norman Feitelson.
Louis Frederick Fieser.
Stanley Knoel Freeman.
Pierre Raoul Gendron.
William Scott Gilbert.
Peter Henry Gore.
Robert Stewart Gow.
Zaky Iskander Hanna.
Stanton Avery Harris.
Ralph Franz Hirschmann.
George Herbert Hitchings.
John James Hobbs.
Harold Theodore Clyde Howard.
Balkrishna Harihar Iyer.
Leslie William Keene.
William Orlin Kenyon.
Nural Absar Khan.
Kenneth Lyall Lee.
Thomas Patrick Maher.
William McPhillamy.
Sorab Siavax Mehta.
Adel Latif Nakhla.
Rajendra Lal Nath.
Michael David Perry.
Daniel Reichenberg.
Frank Roland Richards.
Lewis Edward John Roberts.
James Turner Rudesill.
John Stafford.
Ronald Stiles Stuart.
David Brynmor Thomas.
Ernest William Tapley.
Roger Townsend.
Keren Bridget Tyrrell.
Peter Charles Wailes.
Dennis Charles Wall.
Sharif Uddin Ahmed Warsi.
Gerald Paul Warwick.
Douglas Walker Wiley
Colin Victor Worth.

and the following 48 candidates were elected on September 18th, 1950:

Mohamed Ibrahim Ali.
George Gerald Badcock.
Trevor Hugh Bates.
Sydney George Beech.
Mary Patricia Valerie Boarland.
Melvin Calvin.
John Hardwick Long Champion.
Mustaq Ahmad Chaudhry.
John Derek Cosgrove.
John Newton Counsell.
Frank Crowder.
Drury Norman Davies.
Vance Hayden Dodson, jun.
Lionel Thomas Dowling.
Lennox Rutherford Dunley.
Owen Burchell Edgar.
Zeinab Abu Elela.
Benjamin Gilbert.

William Frederick Graydon.
Noel Arthur Hampson.
Stephen Aven Herbert, jun.
Harry Fred Herbrandson.
Cyril David Hough.
Donald William Hutchings.
Edward Arnould Norman Stanley Jeffries.
Ahmad Kamal.
Irene Violet Rose Kempson.
Lafayette Carroll King.
Alvin Ira Kosak.
Ernest Cecil Leisegang.
Jerrold Meinwald.
Brian Morling.
Richard Joseph Moualim.
Kenneth George Phillips.
Jan Michal Popiel.
C. V. Ramakrishnan.
James Redden.
Tsung-Ying Shen.
Roger Stevens.
William Carl Stickler
Robert Guy Stuart.
Lucie Pauline Torry.
Alan Herbert Turner.
Ernest Edgar Vickers.
Ernest Warhurst.
Leslie Ronald Wilkinson.
Leslie James Wood.
Aaron Arnold Zimmerman.

LOCAL REPRESENTATIVE—NEWCASTLE AND DURHAM.

The resignation of Dr. P. L. Robinson as Local Representative for Newcastle and Durham has been accepted with regret and Dr. G. A. Swan has been appointed as his successor.

CORDAY-MORGAN MEDAL AND PRIZE.

The rules approved by Council governing the award of the Corday-Morgan Medal and Prize were published in the Proceedings for April, 1950, and copies can be obtained from the General Secretary.

Applications and recommendations in respect of the award for 1949, accompanied by the birth certificate of the applicant, must be received not later than December 31st, 1950.

The closing date for the award for 1950 will be December 31st, 1951.

HARRISON MEMORIAL PRIZE.

Applications for the Harrison Memorial Prize for 1950 must be received by the Society not later than December 1st, 1950. The conditions governing the award were given in the Proceedings for May, 1950, and elsewhere.

LIST OF APPLICATIONS FOR FELLOWSHIP

(Fellows wishing to lodge objection to the election of these candidates should communicate with the Honorary Secretaries within ten days of the date of publication of the "Journal" for October, 1950. Such objections will be treated as confidential. The forms of application are available in the Library.)

***Brown, Colin Willcocks,** B.Sc. (Lond.), A.R.I.C. British. 26, Boyd's Walk, Dukinfield, Cheshire. Research Student. *Signed by:* E. Whalley, K. S. W. Sing, E. G. Edwards.

***Burke, Derek Clissold,** B.Sc. (Birm.). British. 43, Four Oaks Road, Four Oaks, Sutton Coldfield. Research Student. *Signed by:* L. L. Bircumshaw, W. Wilson, M. Stacey.

Curtis, Norman Sidney, B.Sc. (Lond.). British. Messrs. Whitbread & Co. Ltd., The Brewery, Chiswell Street, E.C.1. Assistant Biochemist. *Signed by:* B. Meredith Brown, G. Barton Wright, J. T. G. Johnson.

***Duff, Samuel Raymond,** B.A. and B.Sc. (Dublin), A.R.I.C. British. Common Corner, Ballylenaghan, Saintfield Road, Belfast. Research Student. *Signed by:* Wesley Cocker, D. C. Pepper, D. H. Hayes.

***Elmore, Bernard Oscar,** B.Sc. (Lond.). British. 130, Queen Street, Rushden, Northants. Temporary Civil Servant. *Signed by:* Brynmor Jones, R. R. Baldwin, C. Barker.

Findley, George Alec. British. Inglewood, Barkfield Avenue, Formby. Sales and Technical Executive. *Signed by:* R. R. Butler, G. N. Copley, A. E. Findlay, L. H. W. Hallett.

***Foreman, James Kenneth,** B.Sc. (Lond.), A.R.I.C. British. 70, Osborne Road, Willesborough, Ashford, Kent. Scientific Officer, Ministry of Supply. *Signed by:* R. E. Cockaday, H. I. Stonehill, G. I. Goodfellow.

***Gindy, Elhamy Riad,** B.Sc. (Cairo). Egyptian. Department of Fuel Technology, The University, St. Georges Square, Sheffield. 1. Research Student. *Signed by:* Alex H. Lamberton, Jack Barrott, E. Gertrude Turner.

***Herbstein, Frank Herzl,** M.Sc. (Cape Town). South African. Weizmann Institute of Science, Rehovoth. Physicist. *Signed by:* Ernest Bergmann, H. J. E. Loewenthal, David Ginsburg.

***Hoffmann, Arthur Kentaro,** B.Sc. (New York). American. 907, Madison Avenue, New York 21, New York. Research Assistant, Department of Chemistry, Columbia University. *Signed by:* David Curtin, Kenneth B. Wiberg, Alfred P. Wolf.

Ivekovic, Hrvoje, D.Chem.Eng. (Zagreb). Croat. Institute of Inorganic Chemistry, 1, Kukuviceva, Zagreb I, Yugoslavia. Professor. *Signed by:* S. S. Miholic, K. Balenovic, V. Vouk.

Laughton, Paul MacDonell, B.A. (Toronto), M.Sc. (Dalhousie), Ph.D. (Wisconsin). Canadian. c/o Department of Chemistry, Dalhousie University, Halifax, Nova Scotia, Canada. Post-Doctoral Project Associate, University of Wisconsin. *Signed by:* S. M. McElvain, William S. Johnson, Henry J. Schneider.

***Long, James Victor Percival,** M.A. (Cantab). British. 94, Fairfax Road, Teddington. Research Chemist. *Signed by:* F. H. Burstall, G. R. Davies, E. F. G. Herington.

***Lyons, James Michael,** B.Sc. (Aberdeen), A.R.I.C. British. Chemistry Department, Marischal College, Aberdeen. Research Student. *Signed by:* R. B. Strathdee, J. M. C. Thompson, R. H. Thomson.

Ma, Tsu Sheng, B.Sc. (Tsing Hua Univ.), Ph.D. (Chicago). Chinese. Chemistry Department, University of Otago, Dunedin, New Zealand. Senior Lecturer in Microchemistry. *Signed by:* F. G. Soper, J. Murray, W. S. Fyfe.

***Mathias, Anthony Peter,** B.Sc. (Lond.). British. 34, Kilmartin Avenue, Norbury, S.W.16. Research Student. *Signed by:* James Baddiley, E. M. Thain, C. L. Arcus.

Maynard, Joachim, B.Sc. (Lond.). British. c/o Dr. F. Memelsdorff, 1963, Avenida Pueyrredon, Buenos Aires, Argentine. Chemist. *Signed by:* C. W. Picard, H. Bing, H. C. Barany.

***Overton, Karl Howard,** B.Sc., and B.Pharm. (Lond.), Ph.C. British. 43, Braemar Avenue, Wood Green, N.22. Research Chemist. *Signed by:* David J. Drain, George Dunn, B. W. Mitchell.

***Rosenberg, Hanna,** B.Sc. (Lond.), A.R.C.S. British. 15, Exeter Road, N.W.2. Research Student. *Signed by:* Roger Parsons, Lucy F. Oldfield, J. O'M. Bockris.

***Scaife, Jeffrey Sinclair Louis,** B.Sc. (Dunelm). British. 21, Larkhall Rise, Clapham, S.W.4. Chemist, Vacuum Oil Co., Wandsworth. *Signed by:* T. Paterson, H. J. Vipond, B. K. Davison.

Sullivan, Edwin Percy Albert, B.Sc. (Sydney). British. 29, Howard Street, Randwick, Sydney, N.S.W., Australia. Research Assistant, Department of Physical Chemistry, University of Sydney. *Signed by:* R. J. W. Le Fèvre, H. G. Holland, H. C. Freeman.

Swaine, Jack, B.A. and B.Sc. (Oxon). British. 8, South Drive, Chorltonville, Manchester, 21. Research Chemist. *Signed by:* F. G. Jeffers, J. R. Lewis, Z. E. Jolles.

Trotter, Ian Fenwick, M.A. (Oxon). British. c/o Courtaults Ltd., No. 1 Laboratory, Foleshill Road, Coventry. Research Spectroscopist. *Signed by:* C. H. Bamford, H. Paul, E. B. Uvarov.

***Wheeler, Owen Howard,** A.R.C.S. British. Organic Chemistry Department, Royal College of Science, Imperial Institute Road, S.W.7. Research Student. *Signed by:* R. P. Linstead, E. A. Braude, J. E. H. Hancock.

Yoffe, Abraham David, M.Sc. (Melbourne), Ph.D. (Cantab.) British. Department of Physical Chemistry, Free School Lane, Cambridge. Research Scientist. *Signed by:* R. N. Haszeldine, Peter Gray, Alan G. Sharpe.

UNDER SPECIAL PROVISION APPERTAINING TO CANDIDATES RESIDENT ABROAD.

Coetzee, Johannes Francois, M.Sc. (S. Africa). South African. Chemistry Department, University of the Orange Free State, Bloemfontein, South Africa. Lecturer. *Signed by:* P. W. G. Groenewoud.

Koenig, Theodore Anthony, D.Eng.Chem. (Brunswick), B.Sc. and Ph.C. (Munich). A.R.I.C. British. c/o East African Industrial Research Board, P.O. Box 1587, Nairobi, Kenya. Scientific Officer. *Signed by:* W. Colet Birch.

MacGregor, Ian R., A.B., M.Sc., and Ph.D. (Cincinnati). American. Department of Chemistry, University of Cincinnati, Cincinnati 21, Ohio, U.S.A. Professor of Chemistry. *Signed by:* Alvin I. Kosak.

***Nager, Maxwell,** B.Sc. (New York). American. Department of Chemistry, Ohio State University, Columbus 10, Ohio, U.S.A. Graduate Student and Teaching Assistant. *Signed by:* Christopher L. Wilson.

Poshkus, Algirdas Charles, B.S. (Bates Coll.), Ph.D. (Chicago). American. 1156 E. 56th Street, Chicago 37, Illinois, U.S.A. Research Assistant. *Signed by:* R. M. Acheson.

Ralha, Alberto Jose Nunes Correia. Portuguese. Rua Bernardo Lima 50, Lisbon, Portugal. Assistant Master, School of Pharmacy, Uiversity of Lisbon. *Signed by:* R. G. C. da Costa.

Wright, George F., Ph.D. (Iowa State Coll.). Canadian. Chemical Laboratory, University of Toronto, Toronto, Ontario, Canada. Professor. *Signed by:* D. C. Lloyd.

PAPERS RECEIVED

(List of papers received between August 22nd and September 18th, 1950.)

" Refrachor—a new physical constant." By S. S. Joshi and G. D. Tuli.
" The constitution of vaccenic acid." By S. S. Gupta, T. P. Hilditch, S. Paul, and R. K. Shrivastava.
" Simple and complex fluorides of some noble metals." By A. G. Sharpe.
" The crystal structures of the acid salts of some monobasic acids. Part II. Potassium hydrogen bis-*p*-hydroxybenzoate hydrate." By J. M. Skinner and J. S. Speakman.
" Chemistry of New Zealand *Melicope* species. Part VI. A revised constitution for meliternatin, and the identification of xanthoxyletin from the bark of *Melicope ternata*." By Lindsay H. Briggs and R. H. Locker.
" β-Aroylpropionic acids. Part I. The mechanism of the interaction of phenol and succinic anhydride in the presence of aluminium chloride. The nature of the Fries reaction." By F. G. Badder and Lanson S. El-Assal.
" Pteridines. Part I. Pteridine, 2- and 4-amino-, and 2- and 4-hydroxy-pteridines." By Adrien Albert, D. J. Brown, and Gordon Cheeseman.
" The preparation of some naphthafluoranthenes and their quinones." By Neil Campbell, A. Marks, and D. H. Reid.
" Halogenation in the liquid phase by use of chlorine trifluoride." J. F. Ellis and W. K. R. Musgrave.
" Methods of resolution. Part II. (−)-*N*-Menthyl-*p*-sulphonamidobenzoic acid." By (Miss) B. A. Everard and John A. Mills.
" The action of hydroxyl radicals on cholesterol and some of its esters." By G. R. Clemo, M. Keller, and J. Weiss.
" The heterolytic fission of the carbon–iodine bond in trifluoroiodomethane." By (Miss) J. Banus, H. J. Emeleus, and R. N. Haszeldine.
" Studies in peroxidase action. Part V. The oxidation of dimethylaniline." By F. T. Naylor and B. C. Saunders.
" The *Senecio* alkaloids. Part VIII. The occurrence and preparation of the *N*-oxides. An improved method of extraction of the *Senecio* alkaloids." By Matteus J. Koekemoer and Frank L. Warren.
" Synthesis of fluoranthenes. Part V. 11-Methoxyfluoranthene." By John Hawkins and S. Horwood Tucker.
" Synthesis of fluoranthenes. Part VI. Utilization of the Mannich reaction." By H. W. D. Stubbs and S. Horwood Tucker.
" The action of alcohol on phthalic anhydrides." By David Lavie, Yehuda Hirshberg, and Ernst D. Bergmann.
" Potential typanocides of the *N*-heterocyclic series. Part V. Structural conditions for activity against *Trypanosoma cruzi* in the phenanthridine series." By L. P. Walls.
" Nucleotides. Part V. Riboflavin-5′ phosphate." By H. S. Forrest and A. R. Todd.
" Nucleotides. Part VI. The structure of the synthetic nucleotides prepared from the benzylidene ribonucleosides." By D. M. Brown, L. J. Haynes, and A. R. Todd.
" Syntheses with isotopic tracer elements. Part III. The measurement of radioactive carbon (C^{14}) by gas-counting of carbon dioxide." By B. N. Audric and J. V. P. Long.
" The alkalimetric determination of metals with the aid of acid-base indicators." By J. F. Coetzee.
" Colouring matter of the aphididae. Part IV. A general survey of the occurrence of the aphins." By H. Duewell, J. P. E. Human, A. W. Johnson, S. F. MacDonald, and A. R. Todd.
" Some physical properties associated with ' aromatic ' electrons. Part III. The pseudo-metallic properties of graphite–potassium and graphite–bromine." By F. R. M. McDonnell, R. C. Pink, and A. R. Ubbelohde.

" Researches on acetylenic compounds. Part XXVIII. A new route to diacetylene and its symmetrical derivatives." By J. B. ARMITAGE, E. R. H. JONES, and M. C. WHITING.

" Researches on acetylenic compounds. Part XXIX. The reaction between nickel carbonyl and disubstituted acetylenes." By E. R. H. JONES, T. Y. SHEN, and M. C. WHITING.

" The synthesis and properties of 2 : 4-diaminothiazoles." By W. DAVIES, J. A. MACLAREN, and L. R. WILKINSON.

" Determination of association in several organophosphorus acids." By G. M. KOSOLAPOFF and J. S. POWELL.

" *p*-Bromophenacyl formate." By JOHN FREDERICK GROVE and P. J. SUTER.

" The formation of complex fluorides. Part II. Reactions in anhydrous hydrogen fluoride and iodine pentafluoride." By A. A. WOOLF.

" A contribution to the chemistry of the sesquiterpene humulene." By G. R. CLEMO and J. O. HARRIS.

" An infra-red spectroscopic investigation of the reaction between acetic anhydride and butyric anhydride." By L. BROWN and I. F. TROTTER.

" Methods of resolution. Part III. Variations of the resolution of alcohols through acid esters." By A. KILLEN MACBETH, J. A. MILLS, and R. PETTIT.

" Contribution to the chemistry of amidone. A study of some isomeric chlorodialkylaminopropanes and their reaction with diphenylmethyl cyanide." By P. Ofner.

" The structure of the mannan present in *Porphyra umbilialis*." By J. K. N. JONES.

" The hydrogenolysis of dithioesters and thioamides." By J. BADDILEY.

" Pyrazine derivatives. Part XII. Synthesis of homologues of aspergillic acid." By D. W. C. RAMSAY and F. S. SPRING.

" Triterpene resinols and related acids. Part XIX. Isolation of a triterpenediol from *Canarium schweinfurthii* resin." By RATNAM BHUVANENDRAM, WILLIAM MANSON, and F. S. SPRING.

" Magnetochemistry of the heaviest elements. Part III. The halides of ter- and quadrivalent uranium." By J. K. DAWSON.

" The oxidation of phenols with benzoyl peroxide. Part II. By STANLEY L. COSGROVE and WILLIAM A. WATERS.

" An acid-catalysed chlorination by means of hypochlorous acid." By W. A. WATERS.

" An induced oxidation of alcohols during the reduction of acid permanganate." By J. H. MERZ, G. STAFFORD, and WILLIAM A. WATERS.

" A method of direct iodination of aromatic compounds." By D. H. DERBYSHIRE and WILLIAM A. WATERS.

" The configuration of (+)-14-methylhexadecanoic acid and homologous *anteiso*-acids." By LESLIE CROMBIE and STANLEY H. HARPER.

" An inexpensive thermostat relay." By DUNCAN TAYLOR.

" The electrolytic dissociation of zinc sulphate, copper sulphate, and zinc malonate in mixed solvents." By J. C. JAMES.

" The dissociation constant of calcium hydroxide." By C. W. DAVIES and BERNARD E. HOYLE.

" Syntheses in the naphthalene series. Part IV. 3-Hydroxy-1 : 4-naphthaquinone-2-acetic acid and its homologues." By GABRA SOLIMAN and (in part) ALBERT LATIF.

" $\alpha\gamma$-Diaminobutyric acid." By S. WILKINSON.

" Diamidides. Part I. Derivatives of triazapentadiene and tetra-azaheptatriene." By F. C. COOPER, M. W. PARTRIDGE, and W. F. SHORT.

" Humic acids from coal. Part I. The humic acids prepared by oxidation with dilute nitric acid with oxygen under pressure." G. H. THOMSON.

" Humic acids from coal. Part II. Condensation reactions." By G. H. THOMSON.

" The oxidation of toluene." By ROBERT DUNCOMBE ABELL.

" A new technique for the reduction of certain heterocyclic methiodides." By J. A. BARLTROP and D. A. H. TAYLOR.

"The caryophyllenes. Part VIII. The synthesis of isocaryophyllenic acid." By T. L. Dawson and G. R. Clemo.

"The constitution of copper peroxide, and the catalytic decomposition of hydrogen peroxide." By Abraham Glasner.

"Chemical actions of ionising radiations in solution. Part VII. Radiation chemistry of sterols. The action of *X*-rays on cholic acid in aqueous solution." By Max Keller and Joseph Weiss.

"Experiments on the preparation of indolocarbazoles. Part II. Some observations on the Graebe–Ullmann carbazole synthesis." By G. G. Coker, S. G. P. Plant, and P. B. Turner.

"The preparation of some di-(2 : 3-epoxy-*n*-propyl)amines." By R. F. Homer.

"The thermal decomposition of dihydroascaridole." By C. G. Moore.

"The reaction of di-*tert.*-butyl peroxide with cyclic and acyclic monoketones." By C. G. Moore.

"The chloroethoxides of zirconium." By D. C. Bradley, F. M. Abd el Halim, and W. Wardlaw.

ADDITIONS TO THE LIBRARY

I. *Donations*

Colonial Geological Surveys. Colonial Geology and Mineral Resources. Vol. 1, etc. London 1950 +. (*Reference.*)

Colonial Products Advisory Bureau (Plant and Animal). Colonial Plant and Animal Products. Vol. 1, etc. London 1950 +. (*Reference.*)

Dyson, G. M. A manual of organic chemistry for advanced students. Vol. 1. The compounds of carbon, hydrogen, oxygen and the halogens. London 1950. pp. xiv + 984. (*Reference.*) Longmans. 63*s*.

From the Author.

Grubitsch, H. Anorganisch-präparative Chemie. Arbeitsmethoden und ausgewähle Beispiele. Wien 1950. pp. xxiii + 479. ill. $7.

From the Publishers: Messrs. Springer-Verlag.

McCrae, J. A chronologically arranged list of people concerned in the development of chemistry. Johannesburg 1950. pp. [iv] + 49 + 7. (*Reference.*) [Typescript.]

From the Author.

Ministry of Supply. Selected Government Research Reports. Vol. 7. Adhesives. London 1950. pp. [iv] + 89. ill. H.M.S.O. 7*s*. 6*d*. (*Recd.* 11/9/50.)

From the Board of Trade.

Progress in Biophysics and Biophysical Chemistry. Vol. 1. Edited by J. A. V. Butler and J. T. Randall. London 1950. pp. viii + 279. ill. 50*s*. (*Recd.* 5/8/50.)

From the Publishers: Messrs. Butterworth-Springer, Ltd.

Sweeney, W. J. Petroleum and its products. (24th Annual Priestley Lecture, Pennsylvania State College.) Pennsylvania 1950. pp. vii + [142]. ill. (*Reference.*)

From the Bureau of Abstracts.

Wiggin, Henry, & Co., Ltd. Monel and some other high-nickel alloys versus sulphuric acid. Birmingham [1950]. pp. 71. ill.

From the Director.

II. *By Purchase*

Eiweiss-Forschung. Abhandlungen aus dem Gebiet der Proteine. Vol. 1, etc. Hamburg 1948 +. (*Reference.*) H. A. Keune Verlag.

Euler, H. von, and Hasselquist, H. Reduktone: Ihre chemischen Eigenschaften und biochemischen Wirkungen. (Sammlung, N.F. Heft 50.) Stuttgart 1950. pp. iv + 55. ill. (*Reference.*) Enke. *DM*. 6.90.

Ferényi, J. Die Filtration mit aktivierten Kieselguren: Ein Berater für die Praxis. (Sammlung, N.F. Heft 46.) Stuttgart 1941. pp. 120. (*Reference.*) Enke. *DM*. 9.40.

Frear, D. E. H. [Editor]. Agricultural chemistry. Vol. 1. Principles. New York 1950. pp. viii + 812. ill. Van Nostrand. $9. (*Recd.* 13/9/50.)

Kellogg, M. W., Co. Technical data book. Liquid vapour equilibrium in mixtures of light hydrocarbons. M. W. Kellog equilibrium constants. Polyco data. New York 1950. pp. 5 + 192 charts. (*Reference.*) $20.

Moritz, H. Spektrochemische Betriebsanalyse. (Die chemische Analyse. Vol. 43.) Stuttgart 1946. pp. xi + 170. ill. (*Reference.*) Enke. 33*s*.

Peters, G. Die hochwirksamen Gase und Dämpfe in der Schädlingsbekämpfung.

(Sammlung, N.F. Heft 47a.) Stuttgart 1952. pp. 143. ill. (*Reference.*) Enke. *DM.* 9.40.

SCHARRER, K. Die biochemischen Grundlagen der Tierernährungslehre. (Sammlung, N. F. Heft 51.) Stuttgart 1950. pp. viii + 162. ill. (*Reference.*) Enke.

TIMMERMANS, J. Physico-chemical constants of pure organic compounds. Amsterdam 1950. pp. viii + 693. (*Reference.*) Elsevier. 95*s.*

VOGEL, H. Chemie und Technik der Vitamine. (Sammlung, N. F. Heft 45.) Stuttgart 1943. pp. xii + 351. ill. (*Reference.*) Enke. *DM.* 16.

WALDSCHMIDT-LEITZ, E. Chemie der Eiweisskörper. (Sammlung, N. F. Heft 49.) Stuttgart 1950. pp. vii + 187. ill. (*Reference.*) Enke. *DM.* 16.

III. *Pamphlets*

BECHERT, C., Sur la théorie de la propagation des combustions, avec une application à la combustion de l'ozone. (From *Portug. Phys.*, 1949, **3**.) pp. [62].

BIOCHEMICAL SOCIETY. Symposium No. 5. Biological oxidation of aromatic rings. Edited by R. T. WILLIAMS. Cambridge 1950. pp. [vi] + 96. ill. [Two copies.] Camb. Univ. Pr. 8*s.*

BRITISH COKING INDUSTRY ASSOCIATION, COUNCIL OF IRON PRODUCERS, and BRITISH IRON AND STEEL FEDERATION. *Joint Coke Consultative Committee.* Recommended methods for the sampling and determination of moisture in coke, at coke ovens and blast furnaces (Report of the South Yorkshire Coke Quality Panel). London 1950. pp. vi + 17. ill.

GILLIS, J. Electrodenpotentialen in waterige oplossing. (From *Meded. Vlaamse Chem. Ver.*, 1949, **11**.) pp. [19].

IVEKOVIĆ, H., and ASPERGER, S. Konduktometrijsko odredivanje ugljicnog dioksida. (From *Rad Jug. Akad. Znan. Umj.*, [1949], **276**.) pp. 27. ill.

—— and MIKIĆ, F. O primjeni statistickih metoda u analitickoj kemiji. (From *Rad Jug. Akad. Znan. Umj.*, [1948], **271**.) pp. 23. ill.

—— —— Application des méthodes statistiques dans la chimie analytique. (From "*Rad*" *de l'Acad. Yougoslave*, [1948], **271**.) pp. 12. ill.

KARSULIN, M., TOMIĆ, A., and LAHODNY, A. Studije o boksitima. (From *Rad Jug. Akad. Znan. Umj.*, [1949], **276**.) pp. 18. ill.

NATIONAL DISTILLERS CHEMICAL CORPORATION. Sodium. New York 1949. pp. 50. ill.

ROSS, S. The inhibition of foaming: the theory of foam inhibition by insoluble antifoaming agents and a review of current industrial problems and practices. (*Rensselaer Polytech. Inst. Bull., Eng. and Sci. Ser.*, 1950, No. 63.) pp. iii + 40.

ROYAL INSTITUTE OF CHEMISTRY. Lectures, Monographs and Reports 1950, No. 3. The synthesis of purine nucleotides. By J. BADDILEY, and The synthesis of some natural products by the use of acetylenic precursors. By R. A. RAPHAEL. (3rd and 4th Meldola Medal Lectures.) London 1950. pp. ii + 31. ill. [Two copies.]

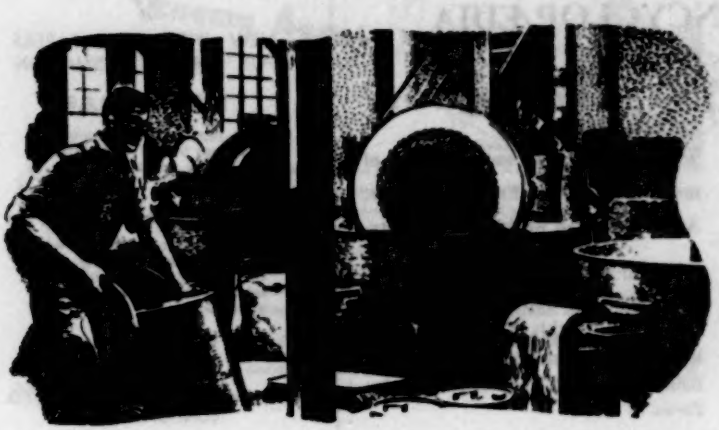
SORNET, R. Le plomb tétraéthyle: roi des antidétonants. Ses propriétés antichoc expliquées par la catalyse et la relation qui existe entre la structure et la détonance des hydrocarbures aliphatiques saturés. [Drancy 1950.] pp. 23. ill.

UNITED STATES. *Department of Commerce.* National Bureau of Standards. Miscellaneous Publication 196. Nomograms for obtaining the compound composition of hydrated limes from the oxide analysis. By E. M. LEVIN. Washington 1949. pp. ii + 5.

LOCAL REPRESENTATIVES OF THE CHEMICAL SOCIETY.

Aberdeen.	J. M. C. Thompson, M.A., D.Phil., F.R.I.C., Chemistry Department, Marischal College, The University, Aberdeen.
Australia.	T. Iredale, D.Sc., F.R.I.C., The University, Sydney, Australia.
Birmingham.	L. L. Bircumshaw, M.A., D.Sc., Department of Chemistry, The University, Edgbaston, Birmingham, 15.
Bristol.	F. H. Pollard, B.Sc., Ph.D., A.R.I.C., Chemistry Department, The University, Woodland Road, Bristol.
Cambridge.	B. Lythgoe, Ph.D., Organic Chemistry Department, The University, Cambridge.
Canada.	W. D. McFarlane, M.A., Ph.D., The Laboratories, The Canadian Breweries Ltd., 496, Queen Street East, Toronto, 2, Canada.
Ceylon.	M. U. S. Sultanbawa, B.Sc., A.R.I.C., Department of Chemistry, The University, Colombo, Ceylon.
Edinburgh.	N. Campbell, D.Sc., Ph.D., Chemistry Department, King's Buildings, West Mains Road, Edinburgh.
Exeter.	S. J. Gregg, Ph.D., A.R.C.S., F.R.I.C., Department of Chemistry, Washington Singer Laboratories, Prince of Wales' Road, Exeter.
Glasgow.	J. C. Speakman, M.Sc., Ph.D., Chemistry Department, The University, Glasgow, W.2.
Hull.	Professor Brynmor Jones, Sc.D., Ph.D., F.R.I.C., University College, Hull.
India.	Sir Shanti S. Bhatnagar, O.B.E., D.Sc., F.R.S., Council of Scientific and Industrial Research, New Delhi, India.
Irish Republic.	V. C. Barry, D.Sc., F.R.I.C., Medical Research Council of Ireland, The Laboratories, Trinity College, Dublin.
Leeds.	P. A. Briscoe, B.Sc., A.R.I.C., Organic Chemistry Department, The University, Leeds, 2.
Liverpool.	W. B. Whalley, B.Sc., Ph.D., F.R.I.C., Organic Chemistry Department, The University, Liverpool.
"	L. A. Haddock, M.Sc., F.R.I.C., Imperial Chemical Industries, Ltd., Research Department, Widnes Laboratory, Widnes.
Manchester.	G. R. Barker, B.Sc., Ph.D., Chemistry Department, The University, Manchester, 13.
"	M. A. T. Rogers, B.Sc., Ph.D., A.R.I.C., Imperial Chemical Industries, Ltd., Hexagon House, Blackley, Manchester.
Newcastle and Durham.	G. A. Swan, B.Sc., Ph.D., F.R.I.C., Department of Chemistry, King's College, Newcastle-on-Tyne, 1.
New Zealand.	Professor F. G. Soper, C.B.E., D.Sc., Ph.D., F.R.I.C., University of Otago, Dunedin, New Zealand.
Northern Ireland.	H. Graham, D.Sc., A.R.I.C., 26, Malone Hill Park, Belfast.
North Wales.	W. Rogie Angus, M.A., D.Sc., Ph.D., F.R.I.C., Department of Chemistry, University College of North Wales, Bangor.
Nottingham.	D. O. Jordan, M.Sc., Ph.D., A.R.I.C., The University, University Park, Nottingham.
Oxford.	W. A. Waters, M.A., Sc.D., F.R.I.C., Balliol College, Oxford.
Pakistan.	M. I. D. Chughtai, M.Sc.Tech., Ph.D., A.R.I.C., Punjab University Institute of Chemistry, The Mall, Lahore, Pakistan.
St. Andrews and Dundee.	H. T. Openshaw, M.A., D.Phil., Chemistry Department, United College, St. Andrews.
Sheffield.	A. H. Lamberton, B.Sc., Ph.D., Chemistry Department, The University, Sheffield, 10.
South Africa.	Professor W. Pugh, Ph.D., B.Sc., F.R.I.C., Chemistry Department, University of Cape Town, Rondebosch, S. Africa.
Southampton.	K. R. Webb, B.Sc., Ph.D., A.R.I.C., University College, Southampton.
South Wales.	Professor C. W. Shoppee, Ph.D., D.Sc., D.Phil., A.R.C.S., F.R.I.C., University College, Singleton Park, Swansea.

M&B LABORATORY CHEMICALS IN THE SERVICE OF INDUSTRY



Behind the manufacture of paints, dyestuffs and many other industrial products lies a continuous campaign, conducted in the laboratories of the industries concerned, to control, develop and perfect.

May & Baker offer a range of some five hundred laboratory chemicals produced to specifications to meet the requirements of all normal laboratory procedures.

The widespread acceptance of M&B Laboratory Chemicals in every branch of industry bears eloquent testimony to their value.

A complete brochure of specifications will be sent on request.

CH18

MAY & BAKER LTD DAGENHAM Phone: Ilford 3060 Extension 10

THE NEW CHAMBERS'S ENCYCLOPÆDIA

Completely New!

The only post-war encyclopaedia of major status in the English language. A newly written work in its entirety.

"IN range, clearness of conception, weight of authority and liberality of mind this is in every way a historic achievement." — Master of Balliol (Sir David Keir) in *The Sunday Times*.

YOU will find that the new CHAMBERS'S ENCYCLOPÆDIA is something you have always wanted. You will spend hours of delight just reading its pages wherever your mood takes you, although its greatest value to you will be found in the up-to-date information, unimpeachable in authority and scholarship, immediately available at your elbow.

SEND TODAY FOR A COMPLETE PRE-VIEW

AS a first step to discovering that this outstanding publishing achievement will cost you far less than you have hitherto paid for a major work of this scope, send this coupon for free illustrated brochure NOW.

GEORGE NEWNES LTD. (CS.1), 136-137, Long Acre, London, W.C.2.

Please send me free and without obligation your illustrated brochure containing a complete survey of contents, together with information of your publication offer for sets of the first printing.

Full Name _____
(Please give exact title, rank, Mr., Mrs., or Miss.)

Profession _____ *Householder?* _____

Address _____

_____

_____

See the Chambers's brochure before you order any other encyclopaedia.

NEW INDICATOR PAPERS FOR *p*H DETERMINATION

UNIVERSAL

One paper covering completely the range from 1 to 10 enabling *p*H values to be checked to within 0·5 *p*H.

COMPARATOR

Four separate books for work requiring greater accuracy. With these papers the *p*H value of any solution can be ascertained to within 0·3 *p*H.

Descriptive leaflet will be sent free on request

JOHNSONS OF HENDON LTD.
LONDON, N.W.4

ACID-PROOFING

A COMPREHENSIVE ORGANISATION FOR ALL TRADES & INDUSTRIES

ACID-RESISTING FLOORS
TANKS AND LININGS OF
ALL KINDS

Backed by 25 years' experience

PRODORITE LTD.

HEAD OFFICE & WORKS: WEDNESBURY, STAFFS.
Telephone: 0284 (five lines)
London Office: Artillery House, Artillery Row, S.W.1
Telephone: Abbey 3816 (five lines)

... is at the bottom of many a case of industrial sabotage. Corrosion of metals, deterioration of chemicals, clogging of fine powders, irregularities in control instruments and countless other troubles in plant and products can be traced to moisture in the wrong place.

Fortunately, simple and effective counter-measures can be taken by installing BIRLEC-Lectrodryers. These efficient, self-contained, economical units will maintain low atmospheric humidity in workrooms and stores or will dry compressed air and industrial gases with little or no attention and very moderate cost.

BIRLEC LTD · ERDINGTON · BIRMINGHAM 24

In Australia: Birlec Limited, Sydney, N.S.W.

BIRLEC

L. LIGHT & CO. LTD.

WRAYSBURY nr. STAINES
MIDDLESEX · ENGLAND

Telephone: Wraysbury 43 & 137

Phytol	5/- G	Aurine tricarboxylic acid (ammonium salt)	9/- D
Oxamide	11/- H	Phenol phthlein diphosphate, Na salt	7/- D
Creatine	7/- D	Aluminium *iso*-propoxide (500 g. tins)	80/- K
Carbazole	90/- K	Sulpho-bromphthalein, sodium salt	9/- G
Quercitrin	19/- D	Hexa-hydro-3-hydroxy diphenyl	37/- H
Quinic acid	37/- H	Hexa-hydro-4-hydroxy diphenyl	45/- H
DL-Methionine	45/- H	n-Heptylamine (10 g. ampoules)	35/- D
Benzidine (99%)	52/- K	Allyl *cyclo*hexane propionate	45/- H
2-Amino pyridine	30/- H	α-Methyl-naphthalene (pure)	25/- H
Sodium gentisate	37/- H	Aluminium *tert.*-butoxide	25/- H
Dibenzoyl methane	9/- D	p-Methyl*cyclo*hexanone	12/- H
p-Amino-azo-benzene	8/- H	p-Methyl *cyclo*hexanol	8/- H
*cyclo*Octa-tetra-ene	20/- G	1 : 4-Diphenyl butadiene	4/- G
Dihydrazine sulphate	11/- H	α-Phenyl-n-butyramide	12/- H
Dibenzoyl disulphide	42/- H	α-Naphthol phthalein	56/- D
1 : 3-*cyclo*Hexane-dione	68/- H	Palmitic acid (90%)	30/- K
Propylene chlorhydrin	62/- K	o-Hydroxy-diphenyl	9/- H
Hexa-hydro-o-toluidine	6/- D	p-Hydroxy-diphenyl	35/- K
Hexa-hydro-m-toluidine	7/- D	Thiodibutyric acid	12/- H
Methane-sulphonic acid	30/- H	Thymol phthalein	10/- G
Rubidium carbonate (90%)	80/- D	Bromo-phenol red	40/- D
5-Nitro-1 : 10-phenanthroline	30/- G	Picrolonic acid	10/- D
3-Dimethyl-amino-propylamine	7/- D	Picolinic acid	12/- D
β-Dimethyl-amino-propionitrile	9/- D	Gentisic acid	47/- H
β-Naphthalene-sulphonechloride	28/- H	Phloridzin	13/- D
2-Bromo-ethylamine hydrobromide	30/- H	L-Cystine	56/- K
Itaconic anhydride (10 g. ampoules)	15/- D	Quercetin	13/- D
1 : 5-Dihydroxy-2 : 6-dibromonaphthalene	30/- H	Anthrone	9/- D
2 : 2-Dihydroxy-diphenyl (*ortho*'-diphenol)	30/- H	Uracil	17/- D

WHATMAN FILTER PAPERS

Made in England by
W. & R. BALSTON LTD.,
MAIDSTONE, KENT.

FOR CHROMATOGRAPHY

It has now become standard practice to use WHATMAN filter papers for this comparatively new method of analysis. We specially recommend WHATMAN grades Nos. 1, 3MM, 4, 7, 11 and 54, which have proved eminently suitable for this type of work. All these grades can be obtained in convenient size sheets from laboratory furnishers. In case of any difficulty in obtaining supplies quickly, please write to the Sole Mill Representatives :-

H. REEVE ANGEL & CO. LTD., 9 Bridewell Place, London, E.C.4

BISOL — **ORGANIC CHEMICALS**

ACETALS
Dimethyl
Diethyl

ACETATES
Methyl
Ethyl
Isopropyl
Butyl
Amyl

ACETIC ACID
A.R. Grade
Glacial B.P.
Glacial commercial
80% Pure
80% Technical

ACETIC ANHYDRIDE

ACETINS
Monacetin
Diacetin
Triacetin

ACETOACETANILIDE

ACETOACETIC ESTERS
Methyl
Ethyl
Ethyl, sodium salt

ACETONE

ALCOHOLS
Butyl
Amyl
Diacetone
2-Ethyl hexyl

ALCOHOL DENATURANTS
of Wood Naphtha type
Crotonaldehyde

ALDEHYDE AMMONIA

ALDEHYDES
Acetaldehyde
Aldol
Butyraldehyde
Crotonaldehyde
Monaldehyde
Paraldehyde

CITRATES
Tributyl
Triamyl

DIBUTYL ETHER

LACTATES
Ethyl
Butyl
Amyl

MESITYL OXIDE

METHYL ETHYL KETONE

OLEATES
Ethyl
Isopropyl
Butyl

OXALACETIC ESTER
Sodium Salt

OXALATES
Diethyl
Dibutyl

PHTHALATES
Dimethyl
Dimethyl glycol
Diethyl
Dibutyl
Diamyl
Dioctyl
Dinonyl

TARTRATES
Diethyl
Dibutyl

SEBACATES
Dibutyl
Dioctyl

SPECIAL SOLVENTS
Labosol F.S.
Labosol M.A.
Labosol M.Y.S.
Labosol S.S.
Labosol E.13

STEARATES
Butyl
Amyl

BRITISH INDUSTRIAL SOLVENTS LTD.
4 CAVENDISH SQUARE, LONDON, W.1 · PHONE: LANGHAM 4501 · CABLES: 'BISOLV', LONDON
T.A. 35515

LEWIS'S BOOKS ON THE CHEMICAL AND ALLIED SCIENCES

Scientific and Technical Books :: Large Stock of Recent Editions :: Catalogue on request
Foreign Books not in stock obtained under Special Licence

THE SECONDHAND DEPARTMENT at 140 GOWER STREET contains a large stock of scientific and technical literature, both modern and historical; periodicals, etc. Out of print items are sort for and reported free of charge.

BOOKS BOUGHT:—Lists submitted should give author, short title, and date of publication.

H. K. LEWIS & CO. Ltd., 136 Gower Street, London, W.C.1
Business hours: 9 a.m. to 5 p.m., Saturdays to 1 p.m. Telephone: EUSton 4282 (7 lines)

AT REIGATE

OUR JOB

AS ESSENCE MANUFACTURERS

IS TO TAKE NATURAL PRODUCTS WHICH HAVE A FLAVOUR OR AROMA OR BOTH; EXTRACT FROM THEM THE PRINCIPLES RESPONSIBLE FOR THAT FLAVOUR AND AROMA, AND THEN PREPARE THESE PRINCIPLES IN SUCH A FORM AS TO BE EASILY AND CONVENIENTLY AND ECONOMICALLY USED BY OUR CUSTOMERS.

WE ARE SPECIALISTS IN THIS FIELD AND CAN OFFER GUARANTEED NATURAL PRODUCTS WHICH FOR QUALITY AND TRUE FLAVOUR ARE IN A CLASS BY THEMSELVES.

REIGATE BRAND—

VANILLA NATURA
GRAPEFRUIT NATURA
ORANGE NATURA
(SWEET OR BITTER)
ORRIS NATURA

WHITE, TOMKINS & COURAGE, LTD.
NORTH ALBERT WORKS, REIGATE

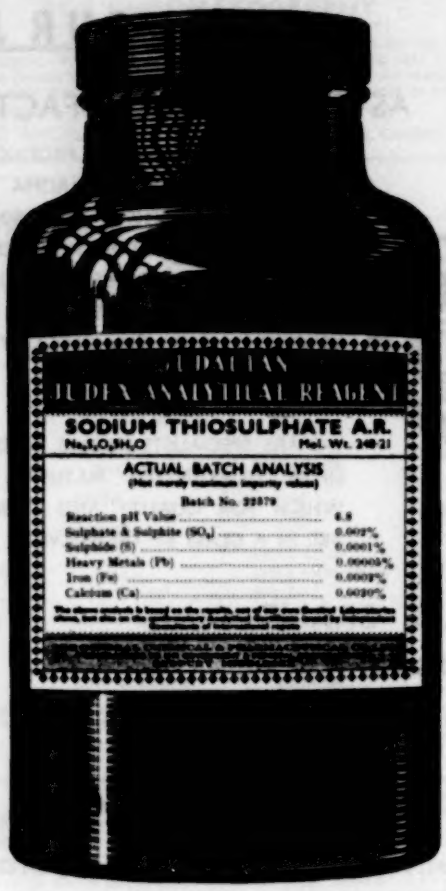
TELEGRAMS: ESSWHITE, REIGATE TELEPHONE: REIGATE 2242-3

ESTABLISHED 1841

JUDACTAN

ANALYTICAL REAGENTS WITH ACTUAL BATCH ANALYSIS

ACTUAL BATCH ANALYSIS



Each batch subjected to INDEPENDENT ANALYSIS before label is printed

You are invited to compare the above actual batch analysis with the purities guaranteed by the specifications of any competing maker in this country or abroad.

THE GENERAL CHEMICAL & PHARMACEUTICAL CO. LTD.
Chemical Manufacturers, Judex Works, Sudbury, Middlesex

CONTENTS.

PAPERS COMMUNICATED TO THE CHEMICAL SOCIETY.

General, Physical, and Inorganic.

PAGE

505. Chemistry of Nitronium Salts. Part I. Isolation of Some Nitronium Salts.
By D. R. GODDARD, E. D. HUGHES, and C. K. INGOLD 2559

506. Vibrational Spectra of Ionic Forms of Oxides and Oxy-acids of Nitrogen. Part I. Raman Spectral Evidence of the Ionisation of Nitric Acid by Perchloric, Sulphuric, and Selenic Acids. Spectroscopic Identification of the Nitronium Ion, NO_2^+.
By C. K. INGOLD, D. J. MILLEN, and H. G. POOLE 2576

507. Vibrational Spectra of Ionic Forms of Oxides and Oxy-acids of Nitrogen. Part II. Raman Spectra of Solutions in Sulphuric Oleum. The Polysulphuric Acids. Ionisation of Nitric Acid in Oleum.
By D. J. MILLEN 2589

508. Vibrational Spectra of Ionic Forms of Oxides and Oxy-acids of Nitrogen. Part III. Raman Spectral Evidence of the Ionisation of Dinitrogen Trioxide, Dinitrogen Tetroxide, and Dinitrogen Pentoxide by Sulphuric Acid.
By D. J. MILLEN 2600

509. Vibrational Spectra of Ionic Forms of Oxides and Oxy-acids of Nitrogen. Part IV. Raman Spectral Evidence of Ionisation in Crystalline Nitronium Salts. The Constitution of Solid Dinitrogen Pentoxide. Note on the Spectrum of the Perchlorate Ion.
By D. J. MILLEN 2606

510. Vibrational Spectra of Ionic Forms of Oxides and Oxy-acids of Nitrogen. Part V. Raman Spectral Evidence of the Ionisation of Dinitrogen Pentoxide in Nitric Acid, and of the Constitution of Anhydrous Nitric Acid.
By C. K. INGOLD and D. J. MILLEN 2612

511. Vibrational Spectra of Ionic Forms of Oxides and Oxy-acids of Nitrogen. Part VI. Raman Spectral Evidence of the Ionisation of Dinitrogen Tetroxide in Nitric Acid. The Nitrosonium Ion, NO^+, and the Nitrosonium–Nitrogen Dioxide Ion, $N_3O_5^+$.
By J. D. S. GOULDEN and D. J. MILLEN 2620

519. Chemical Actions of Ionising Radiations on Aqueous Solutions. Part V. Hydroxylation of Nitrobenzene by Free Radicals produced by *X*-Rays.
By (MISS) H. LOEBL, GABRIEL STEIN, and JOSEPH WEISS 2704

520. Chemical Actions of Ionising Radiations in Solution. Part VI. Radiation Chemistry of Sterols. The Action of *X*-Rays on Cholesterol and 3β-Hydroxypregn-5-en-20-one.
By MAX KELLER and JOSEPH WEISS 2709

526. Studies of Gradual Transitions in Mixed Crystals. Part I. The System Ammonium Chloride–Ammonium Bromide.
By C. J. MANDLEBERG and L. A. K. STAVELEY 2736

529. The Reaction of Diborane with Some Alkene Oxides and Vinyl Compounds.
By F. G. A. STONE and H. J. EMELÉUS 2755

531. The Crystal Structure of Thorium Tetrabromide.
By R. W. M. D'EYE 2764

539. The Formation and Constitution of the Perchromates.
By ABRAHAM GLASNER 2795

546. The Systems Zinc Oxide–Phosphoric Oxide–Water and Manganous Oxide–Phosphoric Oxide–Water at Temperatures between 25° and 100°.
By J. E. SALMON and H. TERREY 2813

563. The Effect of Time and Temperature on Potentials Measured with the Glass Electrode.
By H. IRVING and R. J. P. WILLIAMS 2890

565. The Electrochemical Behaviour of the Antimony Electrode.
By S. E. S. EL WAKKAD 2894

NOTE:

Solvolysis by Bromine Trifluoride.
By A. G. SHARPE 2907

Physical Organic.

		page
512.	Kinetics and Mechanism of Aromatic Nitration. Part VI. The Nitration of Phenols and Phenolic Ethers: the Concomitant Dealkylation of Phenolic Ethers. The Role of Nitrous Acid. By C. A. Bunton, E. D. Hughes, C. K. Ingold, D. I. H. Jacobs, M. H. Jones, G. J. Minkoff, and R. I. Reed	2628
513.	Kinetics and Mechanism of Aromatic Nitration. Part VII. Products of Nitration of Aniline Derivatives, especially of Dimethylaniline. The Concomitant Dealkylation of Dialkylanilines. By J. Glazer, E. D. Hughes, C. K. Ingold, A. T. James, G. T. Jones, and E. Roberts	2657
514.	Kinetics and Mechanism of Aromatic Nitration. Part VIII. The Rearrangement of Aromatic *N*-Nitroamines. By E. D. Hughes and G. T. Jones	2678
525.	A Theoretical Treatment of the Diels–Alder Reaction. Part II. Polyenes, Arylpolyenes, and Related Molecules. By R. D. Brown	2730
545.	The Ultra-violet Spectra of Certain Substituted Aromatic Nitro-compounds. By P. Fielding and R. J. W. Le Fèvre	2812
548.	The Kinetics of Halogen Addition to Unsaturated Compounds. Part XIX. The αβ-Ethylenic Nitriles. By D. A. Evans and P. W. Robertson	2834
549.	The Kinetics of Halogen Addition to Unsaturated Compounds. Part XX. αβ-Unsaturated Sulphones. By I. R. C. McDonald, R. M. Milburn, and P. W. Robertson	2836
550.	The Kinetics of Halogen Addition to Unsaturated Compounds. Part XXI. The Mechanisms of Addition Reactions. By P. B. D. de la Mare and P. W. Robertson	2838
554.	The Associating Effect of the Hydrogen Atom. Part XIV. The Structure of Diacylamines and Related Substances. By Louis Hunter and Norman G. Reynolds	2857
564.	Absorption Spectra and Structure of Organic Sulphur Compounds. Part VII. Sulphoxides. By H. P. Koch	2892

Organic.

515.	Synthesis and Configuration of (+)-6-Methyloctanoic Acid, a Degradation Product of the Polymyxins. By Leslie Crombie and Stanley H. Harper	2685
516.	Organic Fluorides. Part III. Fluorination of Aromatic Hydrocarbons by Use of a Gold Catalyst. By R. N. Haszeldine and F. Smith	2689
517.	The Composition of the Polysaccharide synthesised by *Polytomella caca*. By E. J. Bourne, M. Stacey, and I. A. Wilkinson	2694
518.	Potential Trypanocides of the *N*-Heterocyclic Series. Part IV. 9-Benzoyl- and 9 : 10-Dihydro-phenanthridines. By A. G. Caldwell, F. C. Copp, and L. P. Walls	2698
521.	The Copper-catalysed Decomposition of Aliphatic Diazo-compounds: The Formation of Paraffins of High Molecular Weight. By G. D. Buckley, L. H. Cross, and N. H. Ray	2714
522.	Insecticidal Activity and Chemical Constitution. Part II. Synthesis of Some Analogues of "DDT." By E. John Skerrett and D. Woodcock	2718
523.	Some Chroman and 1 : 2-Benzopyran Derivatives. By Helan V. Taylor and Muriel L. Tomlinson	2724
524.	The Synthesis of Long-chain Aliphatic Acids from Acetylenic Compounds. Part IV. A New Approach to the Synthesis of Branched-chain Acids. By C. L. Leese and R. A. Raphael	2725
527.	Antibacterial Pteridines. 6 : 7-Dialkyl Derivatives of 2 : 4-Diaminopteridine. By N. R. Campbell, J. H. Dunsmuir, and M. E. H. Fitzgerald	2743
528.	Deoxypentose Nucleic Acids. Part I. The Enzymic Degradation of Sodium Deoxyribonucleate by Deoxyribonuclease. By W. G. Overend and M. Webb	2746

PAGE

530. An Unambiguous Synthesis of 3-Aroylflavones and Their Reaction with Benzylamine.
By Wilson Baker and F. Glockling 2759

532. Nuclear Halogen-containing Analogues of Chloramphenicol.
By Ng. Ph. Buu-Hoï, Ng. Hoán, Pierre Jacquignon, and Ng. H. Khoï . . 2766

533. Deoxy-sugars. Part XIII. Some Observations on the Feulgen Nucleal Reaction.
By W. G. Overend 2769

534. New 5-Aminoglyoxalines as Potential Adrenergic Agents.
By H. Bader, J. D. Downer, and (Mrs.) P. Driver 2775

535. The Orientation of Disubstituted Fluoranthene Derivatives.
By Neil Campbell, W. W. Easton, (Miss) J. L. Rayment, and (in part) J. F. K. Wilshire 2784

536. Organic Fluorides. Part IV. Fluorination of Hydroaromatic Hydrocarbons by Use of a Gold Catalyst.
By R. N. Haszeldine and F. Smith 2787

537. The Reactions of Fluorocarbon Radicals. Part III. The Synthesis of Heptafluorobutyric Acid.
By R. N. Haszeldine 2789

538. Organic Fluoro-compounds. Part III. 2 : 4 : 6-Trinitro-3-hydroxybenzotrifluoride—a New Reagent for the Characterisation of Amines and Pyranol Bases.
By W. B. Whalley 2792

540. Reactions of Organic Peroxides. Part III. Oxidation of Methylcyclopentane and Methylcyclohexane.
By E. J. Gasson, E. G. E. Hawkins, A. F. Millidge, and D. C. Quin . . 2798

541. Reactions of Organic Peroxides. Part IV. Reactions of Methylcyclopentyl and Methylcyclohexyl Hydroperoxides.
By E. G. E. Hawkins 2801

542. Reactions of Organic Peroxides. Part V. Reaction of Ferrous Sulphate with Methylcyclopentyl and Methylcyclohexyl Hydroperoxides.
By E. G. E. Hawkins and D. P. Young 2804

543. The Optical Resolution of (±)-*trans*-9 : 10-Dihydroxy-9 : 10-dihydrophenanthrene.
By J. Booth, E. Boyland, and E. E. Turner 2808

544. Allylbenzene Compounds. Part II. 2 : 4 : 6-Trimethoxyallylbenzene.
By P. Holmes, D. E. White, and I. H. Wilson 2810

547. The Synthesis of Thyroxine and Related Substances. Part VII. The Preparation of Diphenyl Ethers from 2 : 6-Di-iodophenols.
By J. H. Barnes, E. T. Borrows, J. Elks, B. A. Hems, and A. G. Long . 2824

551. Synthesis of Potential Antibacterial Agents. Part I. Some α-Alkylglutaric Acids and Their Derivatives.
By John C. Roberts and Bernard Shaw 2842

552. Chemistry of the Vitamin B_{12} Group. Part I. Acid Hydrolysis Studies. Isolation of a Phosphorus-containing Degradation Product.
By J. G. Buchanan, A. W. Johnson, J. A. Mills, and A. R. Todd . . . 2845

553. The Preparation of Dimethyltetrahydrocarbazoles.
By G. Anderson and Neil Campbell 2855

555. The *Euphorbia* Resins. Part V. Oxidative Degradation in the Side Chain of Euphol.
By Hans K. Krüsi 2864

556. The Isolation and Identification of (−)-Stachydrine Ethyl Ester Periodide from the Root of *Courbonia virgata*.
By Alan J. Henry and Harold King 2866

557. The Constituents of the Wood of *Castanospermum australe* Cunn. et Fras. Part I. The Isolation of a New Sapogenin, Castanogenin.
By J. J. H. Simes 2868

558. The Preparation of Tetrahydrocarbazoles from 2-Chlorocyclohexanone.
By Neil Campbell and E. B. McCall 2870

559. Intramolecular Acylation. Part II. The Ring Closure of Some α-Substituted Glutaric Acids.
By M. F. Ansell and D. H. Hey 2874

560. The Steroid Series. Part I. The Ozonolysis of Fucosterol and Some of its Derivatives.
By D. H. Hey, John Honeyman, and W. J. Peal 2881

PAGE

561. The Structure of the Starch-type Polysaccharide Synthesised from Sucrose by *Neisseria perflava*.
By S. A. Barker, E. J. Bourne, and M. Stacey 2884

562. The Synthesis of Neurotropic and Musculotropic Stimulators and Inhibitors. Part IV. Benzilic Acid Derivatives.
By A. L. Morrison, (Miss) M. Königstein, and A. Cohen 2887

566. *trans*-8 : 9-Epoxy-11-ketoheptadecane-1-carboxylic Acid and *cis*-10 : 11-Diketoheptadec-8-ene-1-carboxylic Acid, with Some Observations on the Ultra-violet Absorption Spectra of These and Related Compounds.
By George King 2897

Notes :

The Preparation of Some 1-Chloroalkane-1-carboxylic Acids.
By R. H. Horn, R. B. Miller, and S. N. Slater 2900

Preparation of Some Derivatives of *p*-Hydroxybenzamidine.
By M. W. Partridge 2901

The Reactivity of β-Naphthols and β-Naphthylamines.
By F. Bell and W. H. Hunter 2903

Dinaphthylenes.
By F. Bell and W. H. Hunter 2904

2- and 4-Nitro-3-aminocarbazole.
By George Anderson and Neil Campbell 2904

Sulphanilyl Derivatives of 2-Amino-3 : 6-di-*sec*.-butylpyrazine.
By G. T. Newbold 2905

Preparation of Benzylsuccinic Acid from Ethyl α-Methylcinnamate.
By W. F. Beech and N. Legg 2906

A New Synthesis of Indigo.
By J. Harley-Mason 2907

The Purification of Brucine.
By H. Kacser 2908

Obituary Notices :

Ronald Victor George Ewens 2909

Erich Heymann 2910

Gustav Komppa 2912

Roland Victor Norris 2913

INDEX OF AUTHORS' NAMES.

Anderson, G., and Campbell, N., 2855, 2904.
Ansell, M. F., and Hey, D. H., 2874.
Bader, H., Downer, J. D., and Driver, P., 2775.
Baker, W., and Glockling, F., 2759.
Barker, S. A., Bourne, E. J., and Stacey, M., 2884.
Barnes, J. H., Borrows, E. T., Elks, J., Hems, B. A., and Long, A. G., 2824.
Beech, W. F., and Legg, N., 2906.
Bell, F., and Hunter, W. H., 2903, 2904.
Booth, J., Boyland, E., and Turner, E. E., 2808.
Borrows, E. T. See Barnes, J. H., 2824.
Bourne, E. J., Stacey, M., and Wilkinson, I. A., 2694.
Bourne, E. J. See also Barker, S. A., 2884.
Boyland, E. See Booth, J., 2808.
Brown, R. D., 2730.
Buchanan, J. G., Johnson, A. W., Mills, J. A., and Todd, A. R., 2845.
Buckley, G. D., Cross, L. H., and Ray, N. H., 2714.
Bunton, C. A., Hughes, E. D., Ingold, C. K., Jacobs, D. I. H., Jones, M. H., Minkoff, G. J., and Reed, R. I., 2628.
Buu-Hoï, Ng. Ph., Hoán, Ng., Jacquignon, P., and Khoï, Ng. H., 2766.
Caldwell, A. G., Copp, F. C., and Walls, L. P., 2698.
Campbell, N., Easton, W. W., Rayment, J. L., and Wilshire, J. F. K., 2784.
Campbell, N., and McCall, E. B., 2870.
Campbell, N. See also Anderson, G., 2855, 2904.
Campbell, N. R., Dunsmuir, J. H., and Fitzgerald, M. E. H., 2743.
Cohen, A. See Morrison, A. L., 2887.
Copp, F. C. See Caldwell, A. G., 2698.
Crombie, L., and Harper, S. H., 2685.
Cross, L. H. See Buckley, G. D., 2714.
De la Mare, P. B. D., and Robertson, P. W., 2838.
D'Eye, R. W. M., 2764.
Downer, J. D. See Bader, H., 2775.
Driver, P. See Bader, H., 2775.
Dunsmuir, J. H. See Campbell, N. R., 2743.
Easton, W. W. See Campbell, N., 2784.
Elks, J. See Barnes, J. H., 2824.
El Wakkad, S. E. S., 2894.
Emeléus, H. J. See Stone, F. G. A., 2755.

Evans, D. A., and Robertson, P. W., 2834.
Fielding, P., and Le Fèvre, R. J. W., 2812.
Fitzgerald, M. E. H. See Campbell, N. R., 2743.
Gasson, E. J., Hawkins, E. G. E., Millidge, A. F., and Quin, D. C., 2798.
Glasner, A., 2795.
Glazer, J., Hughes, E. D., Ingold, C. K., James, A. T., Jones, G. T., and Roberts, E., 2657.
Glockling, F. See Baker, W., 2759.
Goddard, D. R., Hughes, E. D., and Ingold, C. K., 2559.
Goulden, J. D. S., and Millen, D. J., 2620.
Harley-Mason, J., 2907.
Harper, S. H. See Crombie, L., 2685.
Hasseldine, R. N., 2789.
Hasseldine, R. N., and Smith, F., 2689, 2787.
Hawkins, E. G. E., 2801.
Hawkins, E. G. E., and Young, D. P., 2804.
Hawkins, E. G. E. See also Gasson, E. J., 2798.
Hems, B. A. See Barnes, J. H., 2824.
Henry, A. J., and King, H., 2866.
Hey, D. H., Honeyman, J., and Peal, W. J., 2881.
Hey, D. H. See also Ansell, M. F., 2874.
Hoán, Ng. See Buu-Hoí, Ng. Ph., 2766.
Holmes, P., White, D. E., and Wilson, I. H., 2810.
Honeyman, J. See Hey, D. H., 2881.
Horn, R. H., Miller, R. B., and Slater, S. N., 2900.
Hughes, E. D., and Jones, G. T., 2678.
Hughes, E. D. See also Bunton, C. A., 2628, Glazer, J., 2657, and Goddard, D. R., 2559.
Hunter, L., and Reynolds, N. G., 2857.
Hunter, W. H. See Bell, F., 2903, 2904.
Ingold, C. K., and Millen, D. J., 2612.
Ingold, C. K., Millen, D. J., and Poole, H. G., 2576.
Ingold, C. K. See also Bunton, C. A., 2628, Glazer, J., 2657, and Goddard, D. R., 2559.
Irving, H., and Williams, R. J. P., 2890.
Jacobs, D. I. H. See Bunton, C. A., 2628.
Jacquignon, P. See Buu-Hoí, Ng. Ph., 2766.
James, A. T. See Glazer, J., 2657.
Johnson, A. W. See Buchanan, J. G., 2845.
Jones, G. T. See Glazer, J., 2657, and Hughes, E. D., 2678.
Jones, M. H. See Bunton, C. A., 2628.
Kacser, H., 2908.
Keller, M., and Weiss, J., 2709.
Khoí, Ng. H. See Buu-Hoí, Ng. Ph., 2766.
King, G., 2897.
King, H. See Henry, A. J., 2866.
Koch, H. P., 2892.
Königstein, M. See Morrison, A. L., 2887.
Krüsi, H. K., 2864.
Leese, C. L., and Raphael, R. A., 2725.
Le Fèvre, R. J. W. See Fielding, P., 2812.
Legg, N. See Beech, W. F., 2906.
Loebl, H., Stein, G., and Weiss, J., 2704.
Long, A. G. See Barnes, J. H., 2824.
McCall, E. B. See Campbell, N., 2870.
McDonald, I. R. C., Milburn, R. M., and Robertson, P. W., 2836.
Mandelberg, C. J., and Staveley, L. A. K., 2736.
Milburn, R. M. See McDonald, I. R. C., 2836.
Millen, D. J., 2589, 2600, 2606.
Millen, D. J. See also Goulden, J. D. S., 2620, and Ingold, C. K., 2576, 2612.
Miller, R. B. See Horn, R. H., 2900.
Millidge, A. F. See Gasson, E. J., 2798.
Mills, J. A. See Buchanan, J. G., 2845.
Minkoff, G. J. See Bunton, C. A., 2628.
Morrison, A. L., Königstein, M., and Cohen, A., 2887.
Newbold, G. T., 2905.
Overend, W. G., 2769.
Overend, W. G., and Webb, M., 2746.
Partridge, M. W., 2901.
Peal, W. J. See Hey, D. H., 2881.
Poole, H. G. See Ingold, C. K., 2576.
Quin, D. C. See Gasson, E. J., 2798.
Raphael, R. A. See Leese, C. L., 2725.
Ray, N. H. See Buckley, G. D., 2714.
Rayment, J. L. See Campbell, N., 2784.
Reed, R. I. See Bunton, C. A., 2628.
Reynolds, N. G. See Hunter, L., 2857.
Roberts, E. See Glazer, J., 2657.
Roberts, J. C., and Shaw, B., 2842.
Robertson, P. W. See De La Mare, P. B. D., 2838, Evans, D. A., 2834, and McDonald, I. R. C., 2836.
Salmon, J. E., and Terrey, H., 2813.
Sharpe, A. G., 2907.
Shaw, B. See Roberts, J. C., 2842.
Simes, J. J. H., 2868.
Skerrett, E. J., and Woodcock, D., 2718.
Slater, S. N. See Horn, R. H., 2900.
Smith, F. See Hasseldine, R. N., 2689, 2787.
Stacey, M. See Barker, S. A., 2884, and Bourne, E. J., 2694.
Staveley, L. A. K. See Mandleberg, C. J., 2736.
Stein, G. See Loebl, H., 2704.
Stone, F. G. A., and Emeléus, H. J., 2755.
Taylor, H. V., and Tomlinson, M. L., 2724.
Terrey, H. See Salmon, J. E., 2813.
Todd, A. R. See Buchanan, J. G., 2845.
Tomlinson, M. L. See Taylor, H. V., 2724.
Turner, E. E. See Booth, J., 2808.
Walls, L. P. See Caldwell, A. G., 2698.
Webb, M. See Overend, W. G., 2746.
Weiss, J. See Keller, M., 2709, and Loebl, H., 2704.
Whalley, W. B., 2792.
White, D. E. See Holmes, P., 2810.
Wilkinson, I. A. See Bourne, E. J., 2694.
Williams, R. J. P. See Irving, H., 2890.
Wilshire, J. F. K. See Campbell, N., 2784.
Wilson, I. H. See Holmes, P., 2810.
Woodcock, D. See Skerrett, E. J., 2718.
Young, D. P. See Hawkins, E. G. E., 2804.

INFORMATION FOR CANDIDATES FOR FELLOWSHIP

The Chemical Society was founded in 1841 and received a Royal Charter in 1848.

The main function of the Society is to foster original research in chemistry and to facilitate the discussion and dissemination of new knowledge in all branches of the science.

Fellowship of the Society is open to men and women of all nationalities who are interested in chemistry and wish to keep in touch with its advances. Fellows are elected by the Council.

PRIVILEGES

Fellows who pay the annual subscription of £3 10s. have the following privileges.

1. To receive a selection of the Society's publications. Publications in excess of those allowed under the Annual Subscription may be purchased at favourable rates. Details are available on application to the General Secretary.
2. To consult and borrow the books in the Library.
3. To attend meetings of the Society both in London and outside London, and to introduce two guests thereto.
4. To apply for research grants.
5. To submit original papers for publication in the *Journal*.

Fellows under the age of 25, who so wish, may pay an annual subscription of £1 15s. and enjoy all the privileges accorded to those paying the full subscription except that the choice of publications is limited.

PUBLICATIONS

(*a*) *The Journal of the Chemical Society*, which is published monthly, contains the results of investigations which cover the whole field of pure chemistry.

(*b*) *British Abstracts*.—The Society collaborates with the Society of Chemical Industry, the Physiological Society, the Biochemical Society, and other organisations in contributing to the maintenance of the Bureau of Abstracts, which issues every month abstracts of papers dealing with all branches of pure and applied chemistry, physiology, and anatomy published in all parts of the world.

British Abstracts A is divided into three sections: AI, General, Physical, and Inorganic Chemistry; AII, Organic Chemistry; AIII, Physiology and Biochemistry, including Anatomy.

(*c*) *Annual Reports on the Progress of Chemistry*.—These reports, written by experts, summarise the important new advances in pure chemistry and related subjects.

(*d*) *Quarterly Reviews* are composed of articles on selected topics from the whole field of chemistry.

LIBRARY

The extensive reference and lending library of the Chemical Society contains over 47,000 volumes dealing with every aspect of chemistry and with many branches of related sciences. The library is open on Monday to Friday from 10 a.m. to 9 p.m., and on Saturdays from 10 a.m. to 5 p.m.

Books available on loan may be sent by post to Fellows residing in Great Britain or Ireland.

MEETINGS

(*a*) *In London*.—Scientific Meetings of the Society are held usually on the first and third Thursdays of each month from October to June at Burlington House, at which papers dealing with original work are read and discussed, organised discussions on subjects of current interest are arranged, and lectures by eminent British and foreign chemists are delivered.

(*b*) *Outside London*.—Scientific Meetings and lectures arranged by the Society's Local Representatives are also held outside London, and form an important part of the activities of the Society.

RESEARCH FUND

A Research Fund is available for the assistance of chemical research, and sums amounting annually to about £700 are granted for this purpose. Application for grants must be made on the appropriate form, which may be obtained from the General Secretary.

Forms of Application for Fellowship can be obtained from THE GENERAL SECRETARY, THE CHEMICAL SOCIETY, BURLINGTON HOUSE, PICCADILLY, LONDON, W.1.

NOTICES TO AUTHORS OF PAPERS

SUBMISSION OF PAPERS. 1. All Scientific Communications for the *Journal* should be addressed to "The Honorary Secretaries, The Chemical Society, Burlington House, W.1." Papers to be read before a meeting of the Society are selected by the Honorary Secretaries.

2. A paper is not normally considered for publication in the *Journal* unless at least one of the authors is a Fellow of the Society, but in exceptional circumstances the Council is prepared to consider papers submitted by non-Fellows.

3. Communications which have appeared or have been accepted for publication with essentially the same scientific content in another Journal or freely available printed work shall not be published in the *Journal* of the Society unless this course is approved by the Council.

4. Papers are accepted by the Society on the understanding that the authors have obtained any necessary authority to publish.

5. The Society reserves the right to retain all papers sent to it, and authors are therefore advised to keep copies. When papers have been accepted for publication the authors are not at liberty, save by permission of the Council, to withdraw or delay them, or to publish them elsewhere until they have appeared in the *Journal* of the Society. Papers which are retained by the Council after being judged unsuitable for publication in the *Journal* are deposited in the Archives of the Society; this right is not usually exercised in regard to illustrations.

MANUSCRIPT. 6. All manuscripts must be top copies, clearly typed, on non-absorbent paper, in double-line spacing and on one side only. Footnotes add considerably to the cost of printing, and should not be used unless necessary.

7. The address to which proofs are to be sent must be given on the front page of every paper.

RESPONSIBILITY. 8. Authors are solely responsible for the factual accuracy of their papers. They are particularly requested to verify references and to indicate positions of cross-references.

SUMMARY. 9. Every paper must be prefaced by a short summary (50—250 words) setting forth briefly and in simple language the objects of the investigation and the results obtained. The summary should give any chemist a clear idea of what the investigation has achieved and should be independent of the main text. "Notes" do not require a summary.

STYLE. 10. Authors are requested to see that their papers conform, as nearly as possible, to the normal style, conventions, and conciseness of the *Journal*.

NOMENCLATURE. 11. Authors are expected to be familiar with the normal rules of nomenclature, but are invited to communicate with the Editor if in doubt or in special cases. Some of the principles followed in the *Journal* are reviewed in "Modern Chemical Nomenclature," by Dr. Clarence Smith (*J.*, 1936, 1067); reprints of this paper may be obtained by Fellows, price 2*d.* post free, from the General Secretary. Much valuable discussion will be found in "British Chemical Nomenclature," by Dr. A. D. Mitchell [Edward Arnold & Co., 1948]. Authors should choose their symbols from the "Report of a Joint Committee of the Chemical Society, Faraday Society, and the Physical Society on Symbols for Thermodynamical and Physico-Chemical Quantities and Conventions Relating to their Use," copies of which may be obtained by Fellows, price 4*d.* post free, from the General Secretary.

NEW COMPOUNDS. 12. New compounds should be indicated by underlining the name at its first mention (excluding headings) in the Experimental section *only*, and by giving analytical results in the form: "Found: ———. ——— requires ———." Analytical results for compounds which have previously been adequately described in the literature should be given in the form: "Found: ———. Calc. for ———: ———."

ILLUSTRATIONS. 13. Illustrations accompanying the papers must be carefully drawn, preferably *twice* the size of the finished block (max. width 5 inches), *in Indian ink, on good white cartridge paper* (graph paper with faint blue lines is acceptable). Any illustration which seriously exceeds four times the size of the finished block will be returned to the author for re-drawing to a smaller scale. Lettering on the drawings, whether on the margin or in the body of the drawing, must not be in ink but must be inserted *clearly but lightly in pencil*. *Margins* of at least two inches must be left. Authors may, if they wish, submit in the first place clearly drawn pencil sketches instead of the completed diagrams, which, however, must be supplied before publication. Further information can be obtained from the Editor.

PROOFS. 14. Authors will be expected to pay the cost of any considerable changes made by them in proof, apart from the correction of printers' errors. See also paragraph 7.

PREPRINTS. 15. Each author, or joint author, receives 10 preprints (without covers) free of charge. A quotation for extra preprints and an order form will be sent with the proofs. The order form (and any necessary remittance) must be returned with the proofs.

505. *Chemistry of Nitronium Salts. Part I. Isolation of Some Nitronium Salts.*

By D. R. Goddard, E. D. Hughes, and C. K. Ingold.

The following crystalline nitronium salts have been prepared in a pure state: (1) nitronium perchlorate, $(NO_2^+)(ClO_4^-)$; (2) nitronium hydrogen disulphate, $(NO_2^+)(HS_2O_7^-)$; (3) nitronium disulphate, $(NO_2^+)_2(S_2O_7^{--})$; (4) nitronium trisulphate, $(NO_2^+)_2(S_3O_{10}^{--})$; and (5) nitronium fluorosulphonate, $(NO_2^+)(FSO_3^-)$. The assigned ionic constitutions are spectroscopically established (Millen) in examples (1), (2), (3), and (5), while the constitution of salt (4) is assumed by analogy. (6) Crystalline dinitrogen pentoxide, which is nitronium nitrate, $(NO_2^+)(NO_3^-)$ (Ingold, Millen, and Poole), belongs to the series, its structure having likewise been spectroscopically established (Chédin; Millen). Nitronium polyselenates have been obtained, but only as mixtures. Nitronium hydrogen sulphate probably has temporary existence as a solid, but it could not be prepared in a pure form, because it passed into nitronium hydrogen disulphate. Nitronium chlorosulphonate could not be obtained, because it decomposed to give nitryl chloride, providing a new route to the preparation of that substance.

Hantzsch's work on the preparation of the alleged salts $(H_2NO_3^{++})(ClO_4^-)$ and $(H_2NO_3^{++})(ClO_4^-)_2$, from nitric acid and perchloric acid, could not be repeated. The following reactions were elucidated in which nitronium perchlorate is formed:

$$HNO_3 + 2HClO_4 = (NO_2^+)(ClO_4^-) + (H_3O^+)(ClO_4^-)$$

$$N_2O_5 + 3HClO_4 = 2(NO_2^+)(ClO_4^-) + (H_3O^+)(ClO_4^-)$$

$$2N_2O_5 + (H_3O^+)(ClO_4^-) \rightleftharpoons (NO_2^+)(ClO_4^-) + 3HNO_3$$

Nitronium hydrogen disulphate was prepared by treating nitric acid with more than two molecular proportions of sulphur trioxide in nitromethane solution, from which the salt crystallised:

$$HNO_3 + 2SO_3 = (NO_2^+)(HS_2O_7^-)$$

The same salt resulted from all attempts to prepare nitronium hydrogen sulphate, apparently because the ions of this salt interact reversibly,

$$2(NO_2^+)(HSO_4^-) \rightleftharpoons (NO_2^+)(HS_2O_7^-) + HNO_3$$

Normal nitronium disulphate was also produced in the reaction between nitric acid and sulphur trioxide, but it could not thus be obtained free from the hydrogen disulphate. It was prepared in a pure form by treating dinitrogen pentoxide with less than two molecules of sulphur trioxide:

$$N_2O_5 + 2SO_3 = (NO_2^+)_2(S_2O_7^{--})$$

Normal nitronium trisulphate was obtained in a pure state when dinitrogen pentoxide was treated with more than three molecular proportions of sulphur trioxide:

$$N_2O_5 + 3SO_3 = (NO_2^+)_2(S_3O_{10}^{--})$$

No more than three molecules of sulphur trioxide could be induced to enter into reaction with dinitrogen pentoxide. The existence of Pictet and Karl's allegedly stable compound, $N_2O_5,4SO_3$, could not be confirmed.

Nitronium fluorosulphonate was prepared from dinitrogen pentoxide and fluorosulphonic acid. Since dinitrogen pentoxide is nitronium nitrate, this reaction may be regarded as a simple anion exchange:

$$N_2O_5 + F{\cdot}SO_2H = (NO_2^+)(F{\cdot}SO_3^-) + HNO_3$$

The corresponding reaction with chlorosulphonic acid did not yield nitronium chlorosulphonate, apparently because the ions of this salt interact, to give nitryl chloride and nitronium hydrogen disulphate:

$$N_2O_5 + Cl{\cdot}SO_2H = (NO_2^+)(Cl{\cdot}SO_3^-) + HNO_3$$

$$(NO_2^+)(Cl{\cdot}SO_3^-) + HNO_3 = NO_2Cl + (NO_2^+)(HSO_4^-)$$

$$2(NO_2^+)(HSO_4^-) = (NO_2^+)(HS_2O_7^-) + HNO_3$$

Chlorine and dinitrogen tetroxide are formed as by-products:

$$N_2O_5 + Cl{\cdot}SO_2H = N_2O_4 + Cl_2 + H_2SO$$

(1) *Origin and Scope.*

(1.1) *Relation of this Paper to Papers of Other Series.*—After it had been established by kinetic studies (*Nature*, 1946, **158**, 448; *J.*, 1950, 2400) that the nitronium ion, NO_2^+, is formed in nitrating media, and when, also, it had been proved by cryoscopic and spectroscopic investigations (*Nature*, 1946, **158**, 480; *J.*, 1950, 2504 and paper no. 508) that the ion can be produced in considerable concentration in solvents such as nitric and sulphuric acids, it seemed obvious that an investigation into the isolation of nitronium salts would be fruitful.

This work has been undertaken in collaboration with Dr. D. J. Millen. Our part has been

to prepare nitronium salts, and to establish their compositions by analysis. His concern has been to prove the presence, or otherwise, of the nitronium ion, and of the anions, in the crystal structures of the compounds, by the method of Raman spectroscopy. His evidence is given in a separate paper (*J.*, 1950, paper no. 509). Geometrically detailed knowledge of the crystal structure of one of the salts is being secured by Prof. E. G. Cox and his collaborators by the method of *X*-ray analysis (cf. *Nature*, 1948, **162**, 159). Dr. R. J. Gillespie has studied the electrolytic properties in solvent sulphuric acid of one of the isolated salts (*J.*, 1950, 2537).

(1.2) ***Guiding Principles of this Work.***—A nitronium salt $(NO_2^+)(X^-)$ may be regarded as an ionised form of the mixed anhydride of nitric acid with the acid HX. We know that, if HX is a very weak acid, such as water, or a moderately weak acid such as benzoic acid, the mixed anhydride, NO_2X is completely covalent. According to Ingold, Millen, and Poole (*Nature*, 1946, **158**, 480; *J.*, 1950, paper no. 509), one ionic nitronium salt has long been known : solid dinitrogen pentoxide is nitronium nitrate, $(NO_2^+)(NO_3^-)$; but, as its high volatility shows, this salt very easily passes into a covalent form. Extrapolating from these indications, we expected that stable nitronium salts would be produced only with the anions of acids which are at least as strong as nitric acid. Several nitronium salts with such anions have now been prepared (cf. *Nature*, 1946, **158**, 480). During the work it was discovered that the strength of an acid is not the only factor which is necessary to confer on its anion a stability sufficient to enable it to resist attack by, so that it may form salts with, the nitronium ion. This will be made clear in the sequel (Sections 3.6 and 4.2).

Perchloric acid has hitherto been considered to be the strongest known acid. Accordingly, our first line of approach to this problem was by way of a revision of Hantzsch's work on the interaction of nitric acid and perchloric acid. Although we shall controvert a number of Hantzsch's conclusions, his central conclusion, *viz.*, that nitric acid on treatment with perchloric acid assumes a cationic form, is confirmed.

Gillespie has pointed out (*J.*, 1950, 2537) that disulphuric acid is a stronger acid than perchloric acid, and also that the higher polysulphuric acids are probably stronger acids still (*J.*, 1950, 2516). Hence we have included the study of nitronium salts with anions of these acids in our programme, as well as with some other stable anions, as is mentioned in the Summary.

(2) *The Reaction between Nitric Acid and Perchloric Acid. The Reaction between Dinitrogen Pentoxide and Perchloric Acid. The Preparation of Nitronium Perchlorate.*

(2.1) ***Outline of Hantzsch's Investigations.***—Hantzsch claimed to have prepared, from anhydrous nitric acid and perchloric acid, two distinct perchlorates, and to have established their compositions by analysis (*Ber.*, 1925, **58**, 958). He called them at first nitronium perchlorate and nitronium diperchlorate, but later nitracidium perchlorate and hydronitracidium perchlorate, respectively. He regarded them as formed by simple proton transfers, as follows :

$$HNO_3 + HClO_4 = (H_2NO_3^+)(ClO_4^-) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (I)$$

$$HNO_3 + 2HClO_4 = (H_2NO_3^{++})(ClO_4^-)_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (II)$$

Hantzsch states (*loc. cit.*) that either salt can be obtained by mixing the component acids in appropriate proportions; and that, by the use of the acids in intermediate proportions, mixtures of the salts are produced, which, by crystallisation from warm nitric acid can be caused to yield the pure monoperchlorate (cf. I), or, by crystallisation from warm perchloric acid, can be completely converted into the diperchlorate (cf. II).

Hantzsch and Berger have given an account of the electrolytic properties of these materials in solution in nitromethane (*Ber.*, 1928, **61**, 1328). They report that the monoperchlorate (cf. I) has a limiting electrical conductivity such as could be expected for a binary electrolyte; and that, during the electrolysis of this salt, nitric acid is transported, as nitracidium ion, towards the cathode. They report also that the diperchlorate (cf. II) has a limiting electrical conductivity appropriate to a ternary electrolyte.

(2.2) ***Comment on Hantzsch's Investigation.***—The point of view from which we commenced our revision of Hantzsch's work was that his nitracidium and hydronitracidium perchlorates, the latter especially, were improbable substances. Our assumption was that the reaction between nitric and perchloric acids was likely to proceed analogously to the cryoscopically and spectroscopically established reaction in solution between nitric acid and excess of sulphuric acid. The solid products would in this case be nitronium perchlorate, and the crystalline monohydrate of perchloric acid, which almost certainly has the ionic constitution of hydroxonium perchlorate :

$$HNO_3 + 2HClO_4 = (NO_2^+)(ClO_4^-) + (H_3O^+)(ClO_4^-) \quad . \quad . \quad . \quad . \quad . \quad (III)$$

This hypothesis necessitates the assumption that Hantzsch's analytical samples were mixtures simulating the compositions of compounds other than any of those which they actually contained. Hantzsch did not prove the homogeneity of the samples analysed, *e.g.*, by fractional crystallisation with a change of solvent. He handled his products in the open laboratory, preparing solids for analysis by draining off the excess of acid on porous tile. The removal of adhering acid must often have been very incomplete, and the interaction with atmospheric moisture considerable.

Most of Hantzsch's recorded analyses agree fairly well with the figures he calculates either for nitracidium perchlorate or for hydronitracidium perchlorate. But he remarks on the difficulty experienced in obtaining good analyses, and it can be read into his account that the recorded figures are not all that were obtained. As will be explained, one is forced to assume this in order to reconcile his description with our hypothesis that the reaction under observation is that represented in equation (III).

It is readily possible on the basis of equation (III) to understand analyses agreeing with the formula of hydronitracidium perchlorate. For, if a mixture of nitronium perchlorate and hydroxonium perchlorate, formed in equimolecular quantities according to equation (III), were to undergo no separation during the preparation of the sample for analysis, then the resulting composition would be identical with that of hydronitracidium perchlorate. On the other hand, it is not possible to understand analyses corresponding to nitracidium perchlorate on the basis of equation (III), except by supposing that a mixture, containing one molecular proportion of nitronium perchlorate and one of hydroxonium perchlorate, also happened to contain one molecular proportion of adhering nitric acid. Hantzsch admits that he did not remove the whole of the adhering acid from his samples by pressing them on porous tile; but the amount remaining should not always have amounted to one molecular proportion; and it should not have been so great, because mixtures containing so much acid are semi-solid pastes.

(2.3) *Revision and Extension of Hantzsch's Investigation.*—Guided by these considerations, the study of the reaction between nitric and perchloric acids was undertaken using all-glass apparatus, so designed that preparations, and all filtrations or other transferences, up to, and including, the weighing for analysis, could be accomplished out of contact with the atmosphere. Later, the reaction between dinitrogen pentoxide and perchloric acid was studied, employing the same type of technique. Temperatures have been kept as low as conveniently possible, in order to minimise the thermal decompositions which anhydrous nitric and perchloric acids, and dinitrogen pentoxide, undergo, and thus to reduce the production of contaminants such as nitrosonium perchlorate.

TABLE I.

Analysis of products formed from nitric acid or dinitrogen pentoxide and perchloric acid. (*Expts.* 1—9).

		AEW.*	*N*, %.	Cl, %.
Required values	$(NO_2^+)(ClO_4^-)$ ...	72·7	9·63	24·4
	$(H_3O^+)(ClO_4^-)$	118·5	0·00	30·0
	$(H_2NO_3^+)(ClO_4^-)$ ...	81·7	8·57	21·7
	$(H_2NO_3^{++})(ClO_4^-)_2$	88·0	5·31	26·9

Expt. no.	Reactants.	Drying time (days).	Analytical results. AEW.*	*N*, %.	Cl, %.	$NClO_3$, %	Assumed $NClO_3$, mol. %	Required for mixtures of $(NO_2^+)(ClO_4^-)$ and $(H_3O^+)(ClO_4^-)$. Calc. AEW.*	*N*, %.
1	$2HNO_3 + HClO_4$	6	87·5	~5·9†	—	—	50·0	88·0	5·31
2	HNO_3 + excess $HClO_4$, washed with $HClO_4$	2	82·6	6·68	—	0·1	64·7	82·6	6·66
3	$HNO_3 + 2HClO_4$, washed with $MeNO_2$	1	75·9	—	—	—	87·0	75·9	—
4	$N_2O_5 + HClO_4$	2	75·5	8·94	—	—	88·7	75·5	8·72
5	$N_2O_5 + HClO_4$, in $MeNO_2$	1	73·7	9·77	—	0·52	95·8	73·7	9·29
6	N_2O_5 + filtrate from $(HNO_3 + 2HClO_4)$ in $MeNO_2$	4	74·7	9·08	—	0·18	91·7	74·7	8·98
7	Excess N_2O_5 + filtrate from $(HNO_3 + 2HClO_4)$ in $MeNO_2$	8	73·0	9·52	—	0·21	98·8	73·0	9·54
8	Solutions of excess N_2O_5 and of $HClO_4$ in $MeNO_2$ mixed	8	72·8	9·47	24·3	—	99·6	72·8	9·59
9	Hantzsch's preparation of $(H_2NO_3^+)(ClO_4^-)$ repeated	7	74·8	9·08	—	0·12	91·8	74·8	8·95

* AEW = acid equivalent weight. † Approximate result.

A chronological summary of the first series of experiments on these lines will now be given, since this seems the simplest way of presenting the evidence concerning the nature of the reactions. Manipulative details are reserved for description in Section 6, but all analyses are reported in Table I. The three types of analysis which have been performed are the acid equivalent weight, the percentage of nitrogen, determined as ammonia by the use of Devarda's alloy, and the percentage of chlorine, determined by the Carius method. Nitrosonium perchlorate, often present in small amount in the samples, was estimated as nitrous acid in aqueous solution by a standard volumetric method.

Expt. 1. Anhydrous perchloric acid (1 mol.) was transferred by non-ebullient distillation at a low pressure and temperature to a bulb already containing anhydrous nitric acid (2 mols.) in solid form at $-80°$. The mixture was warmed to $-40°$, so that the nitric acid melted, and the two acids interacted. The semi-solid product was then vacuum-dried for six days, the temperature being allowed to rise to that of the room as the volatile, liquid material was removed.

Analysis of the dry solid residue (cf. Table I) gave results approximately agreeing with the composition of Hantzsch's hydronitracidium perchlorate $(H_2NO_3^{++})(ClO_4^-)_2$, and therefore also with the composition of the product, $(NO_2^+)(ClO_4^-) + (H_3O^+)(ClO_4^-)$, which should result from the assumed reaction (III), when no opportunity for separation of the components is provided. It is significant that a product of this composition is obtained, not as Hantzsch states to be necessary, by employing initially at least two molecules of perchloric acid to one of nitric acid, but by starting with two molecules of nitric acid to one of perchloric acid. According to Hantzsch, one should in these circumstances, or even if only one molecule of nitric acid is taken to one of perchloric acid, arrive at the monoperchlorate, $(H_2NO_3^+)(ClO_4^-)$. Equation (III) indicates, however, that one would expect to obtain a solid product, which would have the composition of Hantzsch's diperchlorate, but would actually consist of the equimolecular mixture, $(NO_2^+)(ClO_4^-) + (H_3O^+)(ClO_4^-)$, with whatever ratio the nitric and perchloric acids were taken, provided only that, after reaction, only volatile material is removed, no opportunity being allowed for separation of the perchlorates.

Expt. 2. On this occasion the perchloric acid was kept in excess. Anhydrous nitric acid (1 mol.) and perchloric acid (<2 mols.) were mixed by the method used previously, and allowed to react. The solid product, which remained undissolved in the excess of perchloric acid when the mixture had reached the room temperature, was collected on a sintered-glass plate. It was there washed with several further portions of freshly distilled perchloric acid, and finally dried in a vacuum for two days.

This product gave analytical figures (cf. Table I) which agree neither with the requirements of Hantzsch's diperchlorate, nor with those of his monoperchlorate, nor with those of *any* mixture of the two. The figures do, however, correspond to the composition of a mixture of 65 mols. % of nitronium perchlorate and 35 mols. % of hydroxonium perchlorate. According to Hantzsch's view of the reaction, the product should have been pure hydronitracidium perchlorate $(H_2NO_3^{++})(ClO_4^-)_2$, since perchloric acid has been kept in excess. Our interpretation assumes that, as before, the original reaction product was an equimolecular mixture of nitronium perchlorate and hydroxonium perchlorate, but that the filtration and the washing had effected a partial separation by preferentially dissolving out the hydroxonium perchlorate.

Expt. 3. Exploratory tests having shown that hydroxonium perchlorate is readily soluble in nitromethane, an attempt was made to employ this solvent for the separation. The solid product prepared by mixing nitric acid (1 mol.) with perchloric acid (2 mols.) was extracted with successive portions of nitromethane. The first few extracts on cooling to $-20°$ deposited crystals, but the later ones did not; and the residual solid seemed to become less soluble as the extraction was continued. A final residue, amounting to only a small proportion of the solid originally taken for treatment, was dried and analysed. The analysis (Table I) indicated that it contained 87 mols. % of nitronium perchlorate and 13 mols. % of hydroxonium perchlorate.

Expt. 4. Since it appeared that the complete separation of an equimolecular mixture of nitronium and hydroxonium perchlorates by the use of solvents was likely to prove tedious, it was now decided (*a*) to employ dinitrogen pentoxide in place of nitric acid, thereby reducing the proportion of hydroxonium perchlorate initially produced (it can then never be more than 33 mols. %), and (*b*) to decompose as much of that as possible by promoting the second of the following reactions (probably a balanced reaction) by the use of an excess of dinitrogen pentoxide. The expected reactions are as follows, reaction (IV) being analogous to the well-established reaction in solution between dinitrogen pentoxide and excess of solvent sulphuric acid (*J.*, 1950, 2504 and paper no. 508):

$$N_2O_5 + 3HClO_4 = 2(NO_2^+)(ClO_4^-) + (H_3O^+)(ClO_4^-) \quad . \quad . \quad . \quad . \quad . \quad (IV)$$

$$(H_3O^+)(ClO_4^-) + 2N_2O_5 = (NO_2^+)(ClO_4^-) + 3HNO_3 \quad . \quad . \quad . \quad . \quad . \quad (V)$$

Anhydrous perchloric acid was distilled on to an excess of dry dinitrogen pentoxide at $-80°$. The mixture was brought to room temperature and the volatile material was removed by distillation at low pressure for two days. The residue was vacuum-dried. Analysis of the residue gave results (Table I) agreeing with the composition of a mixture of 89 mols. % of nitronium perchlorate with 11 mols. % of hydroxonium perchlorate.

Expt. 5. This experiment was similar except that nitromethane was used as a solvent for the reaction. Anhydrous perchloric acid was distilled into a solution at $-25°$ of an excess of dinitrogen pentoxide in nitromethane. The mixture was allowed to come to room temperature as the volatile material was distilled away with the nitromethane solvent. The residue, after being vacuum-dried

for one day, gave analytical figures (Table I) agreeing with the composition of a mixture containing 96 mols. % of nitronium perchlorate and 4 mols. % of hydroxonium perchlorate.

These results are readily understood on the basis of reactions (IV) and (V), and the expectation that reaction (V) is reversible. For if this is so, reaction (V) cannot be expected to go to completion under the conditions described above, since, on pumping, the residual dinitrogen pentoxide will be removed considerably faster than the nitric acid, the presence of which, coupled with the rapid removal of the dinitrogen pentoxide, will force reaction (V) towards the left.

The obvious counter to this is to remove the dinitrogen pentoxide and nitric acid together by washing with a solvent, which one might so choose that it would wash out also the small amount of remaining hydroxonium perchlorate. This type of principle is employed in the next three experiments, which led to the preparation of pure nitronium perchlorate.

Expt. 6. In the first of them, nitric acid and perchloric acid were brought together in the proportions required by equation (III), in solution in nitromethane, and the formed precipitate was removed by filtration. Then dinitrogen pentoxide was added to the filtrate, in order to convert the hydroxonium perchlorate into nitronium perchlorate, in accordance with equation (V). This led to the formation of another precipitate, which was collected, dried, and analysed. It was thus shown (Table I) to contain 92 mols. % of nitronium perchlorate and 8 mols. % of hydroxonium perchlorate.

Expt. 7. This result proves that, although pure hydroxonium perchlorate is much more soluble in nitromethane than in pure nitronium perchlorate, the former substance has a strong tendency to be co-precipitated with the latter. The obvious reply to this is to have no hydroxonium perchlorate in the solution, *i.e.*, to employ such an excess of dinitrogen pentoxide that reaction (V) is driven completely to the right. Therefore the previous experiment was repeated, but with the use of a considerable excess of dinitrogen pentoxide. The precipitated salt now gave correct analytical figures for nitronium perchlorate (cf. Table I).

Expt. 8. It was realised that the same principles could be applied in a simpler form by using dinitrogen pentoxide throughout as the source of the nitronium ion, instead of nitric acid followed by dinitrogen pentoxide, *i.e.*, by employing reactions (IV) and (V), here summarised in equation (VI), instead of reactions (III) and (V):

$$N_2O_5 + HClO_4 = (NO_2^+)(ClO_4^-) + HNO_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (VI)$$

For the reason explained above, it was necessary to use dinitrogen pentoxide in excess of the quantity indicated to be required by equation (VI). Solutions in nitromethane of perchloric acid (1 mol.) and dinitrogen pentoxide (1·7 mols.) were mixed, and the precipitate was filtered off, washed, and dried. This salt gave good analytical figures for nitronium perchlorate (cf. Table I).

These first eight experiments, and the associated analyses, are reported fully because the complete consistency of the analytical data with the chemical interpretation now offered constitutes, as we think, a convincing case for the latter; even though we have isolated, from the product of the reaction of nitric acid, or of dinitrogen pentoxide, with perchloric acid, only one of the two perchlorates which the interpretation assumes to be formed.

The degree of purity of the *nitronium perchlorate* obtained in experiments 7 and 8 was not less than 99%. Nitrosonium perchlorate was present as an impurity to the extent of about 0·2%. The method of experiment 8 has been used extensively in this laboratory for the preparation of nitronium perchlorate (for details, see Section 5.2).

Expt. 9. We report one further experiment of this series for the following reason. Our interpretation of the reaction between nitric and perchloric acid identifies Hantzsch's supposed hydronitracidium perchlorate, $(H_2NO_3^{++})(ClO_4^-)_2$, as the equimolecular mixture of nitronium and hydroxonium perchlorates which constitutes the total product of the reaction; but it does not identify his reported nitracidium perchlorate, $(H_2NO_3^+)(ClO_4^-)$; and the possibility of his having obtained this substance had to be taken seriously, because it is shown in accompanying papers that the nitracidium ion * can exist at low concentration in somewhat dehydrating conditions (*J.*, 1950, 2400), and that it also exists, not necessarily in very low concentration, in aqueous conditions (*J.*, 1950, 2441). Therefore we directly repeated the preparation described by Hantzsch of his nitracidium perchlorate.

Hantzsch notes that, when anhydrous nitric and perchloric acids are mixed in equimolecular proportions, the product is not completely solid. This is strange if the nitracidium ion is stable enough to form a solid perchlorate. He states that the product must be recrystallised from nitric acid in order to obtain pure nitracidium perchlorate.

We repeated this experiment as exactly as possible. In agreement with Hantzsch's statement, we found that the product obtained by mixing accurately equimolecular proportions of nitric and perchloric acid was only partly solid (though it could be made to go completely solid by adding a second molecular proportion of perchloric acid). The product obtained by mixing the acids in equimolecular proportions was crystallised from nitric acid, and the crystals were filtered, dried, and analysed, as usual. The resulting figures (Table I) do not agree with those obtained by Hantzsch. They also do not agree with the values required for nitracidium perchlorate, or for hydronitracidium perchlorate, or for *any* mixture of these two compounds. They do agree with values calculated for a mixture of

* In this paper we adhere for convenience to Hantzsch's name, "nitracidium" for the cation $H_2NO_3^+$, although in the papers cited in the text the same ion is called the "nitric acidium" ion, for the sake of uniformity with the names of other acidium ions, and particularly to avoid confusion with the nitrous acidium ion, $H_2NO_2^+$.

92 mols. % of nitronium perchlorate with 8 mols. % of hydroxonium perchlorate. The production of such a mixture in these circumstances is entirely consistent with the results and discussion given above.

Our inability to isolate nitracidium perchlorate from mixtures of nitric and perchloric acids containing excess of the former accords with the Raman-spectroscopic result (*J.*, 1950, paper no. 506) that the effect of adding only a few units per cent. of perchloric acid to pure nitric acid is to develop the spectra of the nitronium and perchlorate ions.

(2.4) *The Work of Gordon and Spinks.*—By mixing gas streams containing ozone, nitrogen dioxide, and chlorine dioxide, these authors obtained a white crystalline deposit, of the composition $NClO_4$, which with water gave nitric and perchloric acids (*Canadian J. Res.*, 1940, *B*, **18**, 358). They regarded the compound as formed by association of the radical-oxides, nitrogen trioxide and chlorine trioxide, which they assumed to be produced by the action of ozone on the dioxides: $NO_2 + ClO_2 = NClO_4$. For the product they suggested the covalent structure $O_2N{\cdot}O{\cdot}ClO_2$, with the ionic structure as a possible alternative. Though no identifying physical measurements were made, there seems little doubt that their compound is the same as ours.

(2.5) *Properties of Nitronium Perchlorate.*—This salt forms small, colourless, monoclinic crystals. It decomposes, without exploding, above 135°, giving off nitrogen dioxide.

It is readily soluble in absolute nitric acid, and can be crystallised from the cooled solvent. It is less soluble in nitromethane, but can be crystallised from the warm solvent: a saturated solution in nitromethane at room temperature is about 0·08M. It is still less soluble in chloroform and in carbon tetrachloride: a saturated solution in either of these solvents at room temperature is about 0·01M.

The ionic constitution of the crystalline salt follows from Dr. D. J. Millen's investigation of its Raman spectrum, which he found to consist simply of the superposed spectra of the nitronium ion and of the perchlorate ion (cf. *J.*, 1950, paper no. 509).

As Dr. R. J. Gillespie has shown, the salt dissolves in sulphuric acid to form mainly ionised nitronium hydrogen sulphate and non-ionised perchloric acid, just as ammonium perchlorate dissolves to give principally ionised ammonium hydrogen sulphate and non-ionised perchloric acid (*J.*, 1950, 2537).

The salt is rapidly decomposed by water to form nitric and perchloric acids. For this reason, the crystals cannot be exposed to the atmosphere even for a few seconds without acquiring a coating of acid. But the crystals dissolve in excess of water with only a moderate evolution of heat.

Although nitronium perchlorate reacts violently with many organic compounds, causing ignition and explosions under some conditions, it can be employed in solution in nitromethane for the nitration of aromatic compounds. Benzene is thus converted instantly into nitrobenzene, but nitrobenzene is nitrated only slowly. A study of the kinetics of such nitrations will be reported later.

(3) *The Reaction between Nitric Acid and Sulphur Trioxide. The Reaction between Dinitrogen Pentoxide and Sulphur Trioxide. Preparation of Nitronium Hydrogen Disulphate, Nitronium Disulphate, and Nitronium Trisulphate. Stability of Nitronium Hydrogen Sulphate.*

(3.1) *Reported Compounds from Nitric Acid and Sulphur Trioxide.*—The first account of a crystalline product, formed by the interaction of nitric acid with sulphur trioxide, is that of Weber (*J. pr. Chem.*, 1871, **3**, 336), who assigned to his substance the formula $N_2O_5{\cdot}4SO_3{\cdot}3H_2O$. Hantzsch suggested (*Ber.*, 1925, **58**, 960) that this compound was nitracidium hydrogen disulphate $(H_2NO_3^+)(HS_2O_7^-)$. However, the existence of a substance of this composition has never been confirmed by later workers, and no such compound has been encountered in the present investigation.

Schultz (U.S.P. 1,047,576/1912) and Caster and O'Callaghan (*Ind. Eng. Chem.*, 1932, **24**, 1146) have examined the same reaction. These authors obtained crystalline products, to which they agree in assigning the formula $N_2O_5{\cdot}4SO_3{\cdot}H_2O$. This substance undoubtedly exists; and, as will be noted below, it has the constitution of nitronium hydrogen disulphate, $(NO_2^+)(HS_2O_7^-)$.

The most recently recorded investigation of the reaction between nitric acid and sulphur trioxide is that of Dodé (*Compt. rend.*, 1943, **217**, 153). By dissolving sulphur trioxide in anhydrous nitric acid and cooling the solution to −10°, he obtained crystals of the composition $2N_2O_5{\cdot}3SO_3{\cdot}2H_2O$. He noted that this substance had the curious property of liberating nitric acid, and not dinitrogen pentoxide, on heating; and, indeed, that the crystals appeared to be continuously losing nitric acid at the ordinary temperature, being difficult or impossible to

dry, without change of composition, on that account. On being heated to 90° under reduced pressure, the substance melted, gave off nitric acid rapidly, and resolidified. The solid product thus obtained had the composition $N_2O_5.4SO_3.H_2O$. Evidently this was the compound obtained by Schultz, and by Caster and O'Callaghan, *viz.*, nitronium hydrogen disulphate.

A tentative interpretation of these observations is possible on the following lines. It will be pointed out later that nitronium hydrogen sulphate $(NO_2^+)(HSO_4^-)$, although stable in a dilute solution in a solvent in which the separate ions are stable, is not stable in a concentrated form, because it then undergoes a reaction which may be regarded as a dehydration of the anion by the cation, the products being nitronium hydrogen disulphate and nitric acid :

$$2(NO_2^+)(HSO_4^-) = (NO_2^+)(HS_2O_7^-) + HNO_3$$

If we assume that this reaction, although we know it to proceed fairly easily, is not instantaneous, it might be possible by Dodé's procedure to effect a crystallisation of nitronium hydrogen sulphate before it has had time to decompose completely; or, more probably, to crystallise a mixture of nitronium hydrogen sulphate with some of the nitronium hydrogen disulphate formed from it. If this is the nature of Dodé's first substance, one can understand why the crystals should continue to decompose with loss of nitric acid, and why this reaction should be rapidly completed on heating with the production of pure nitronium hydrogen disulphate. If we may suppose that Dodé's crystals, at the time of their analysis, still contained 75 mols. % of undecomposed nitronium hydrogen sulphate, together with 25 mols. % of nitronium hydrogen disulphate, his analytical results would be explained.

(3.2) *Reported Compound from Dinitrogen Pentoxide and Sulphur Trioxide.*—The only previous report of a compound formed from dinitrogen pentoxide and sulphur trioxide appears to be that of Pictet and Karl (*Compt. rend.*, 1907, **145**, 238). They state that a crystalline precipitate of the composition $N_2O_5.4SO_3$ was formed on mixing solutions of dinitrogen pentoxide and of sulphur trioxide in carbon tetrachloride; and that crystals of the same composition were obtained by dissolving dinitrogen pentoxide in liquid sulphur trioxide, and distilling the product, b. p. 218—220°, which, after solidifying, had m. p. 124—125°.

We have not encountered this compound in the course of our study of the interaction of dinitrogen pentoxide and sulphur trioxide, though we describe two substances which are formed from these oxides, but contain lower proportions of sulphur trioxide.

(3.3) *Reaction between Nitric Acid and Sulphur Trioxide.—Preparation of nitronium hydrogen disulphate.* The general experimental methods which had been developed for the study of the reaction between nitric and perchloric acids were applied to the reaction between nitric acid and sulphur trioxide. When the initially pure substances are mixed, much heat is developed, and side reactions due to decomposition of the nitric acid are difficult to avoid. For this reason, the reaction was conducted in solution in nitromethane. The reactants, each in solution in this solvent, were brought together in various ratios, extending over a 5-fold range; and in all cases colourless, crystalline precipitates were produced, which were collected, usually washed with fresh nitromethane, and dried.

The analyses which were carried out were the acid equivalent weight, the percentage of nitrogen determined as the ammonia formed by reduction with Devarda's alloy, and the percentage of sulphur determined as barium sulphate. A record of the conditions applying to the different experiments, and of all the analytical results, is given in Table II.

Referring first to the column of observed acid equivalent weights, it will be noticed that, for the products of all experiments in which the formed precipitate, after being collected on the filter, was washed with fresh nitromethane before drying (Nos. 12 and 14—18), the acid equivalent weights are identical (44·7), whereas for the products of the two experiments in which the washing with fresh nitromethane was omitted (Nos. 11 and 13) the acid equivalent weights had distinctly higher values (45·5, 45·7). In carrying out these experiments it was noticed that the products of all the preparations in which the washing with fresh nitromethane had been given were obtained as dry, freely flowing, granular powders; but the products of the two experiments in which the washing had been omitted appeared sticky, as though they contained a small amount of some adhering liquid, which could not easily be removed by pumping. On account of these observations we assume that the higher equivalent weights of the products of the experiments in which the extra washing was omitted (Nos. 11 and 13) signalise the presence of other substances than those which we wish at present to discuss.

Let us now consider the whole of the analytical data for the remaining experiments (Nos. 12 and 14—18). The products of all these experiments have the same acid equivalent weight,

TABLE II.

Analysis of products formed from nitric acid and sulphur trioxide.

		AEW.*	N, %.	S, %.
Required values	$N_2O_5.4SO_3.3H_2O$ (Weber)	48·2	5·81	26·6
	$N_2O_5.2SO_3.H_2O = (NO_2^+)(HSO_4^-)$	47·7	9·79	22·4
	$2N_2O_5.8SO_3.2H_2O$ (Dodé)	46·6	8·59	24·6
	$N_2O_5.4SO_3.H_2O = (NO_2^+)(HS_2O_7^-)$	44·6	6·27	28·7
	$N_2O_5.2SO_3 = (NO_2^+)_2(S_2O_7^{--})$	44·7	10·45	23·9
	$N_2O_5.3SO_3 = (NO_2^+)_2(S_2O_{10}^{--})$	43·5	8·04	27·6
	$N_2O_5.4SO_3$ (Pictet and Karl)	42·8	6·54	29·9

Expt. no.	Reactants.	Temp.	Drying (days).	$MeNO_2$ † Washing.	Analytical results. AEW.*	N, %.	S, %.
11	$2HNO_3 + SO_3$	−20°	1·5	−	45·7	7·57	—
12	$2HNO_3 + SO_3$	−20	1·5	+	44·8	8·40	—
13	$1·33HNO_3 + SO_3$	−20	2·5	−	45·5	7·56	—
14	$HNO_3 + SO_3$	−10	1·0	+	44·8	8·40	—
15	$HNO_3 + SO_3$	−10	5	+	44·7	8·43	—
16	$HNO_3 + SO_3$	+20	4	+	44·9	7·96	—
17	$HNO_3 + 2SO_3$	+20	4	+	44·7	6·45	—
18	$HNO_3 + 2·8SO_3$	+20	4	+	44·6	6·26	29·0

* AEW = Acid equivalent weight.

† The symbol + means that the product, precipitated from nitromethane solution, was washed on the filter with fresh nitromethane before being dried; and − means that this washing was not given.

although their nitrogen contents are distributed over a considerable range. This can only mean that the samples consist either of one, or of mixtures of both, of two substances having coincident equivalent weights. In the list at the top of the Table one finds that there are two substances which have a common equivalent weight; and, moreover, that this common value is identical with the value uniformly given by the experiments. The substances concerned are *nitronium hydrogen disulphate*, $(NO_2^+)(HS_2O_7^-)$, and normal *nitronium disulphate* $(NO_2^+)_2(S_2O_7^{--})$, and we assume that they are the components of our substances.

The formation of nitronium hydrogen disulphate may be stoicheiometrically represented as follows:

$$HNO_3 + 2SO_3 = (NO_2^+)(HS_2O_7^-)$$

As is shown by the list of nitrogen determinations given in Table II, one obtains, consistently with this equation, pure nitronium hydrogen disulphate when, and only when, not less than two molecular proportions of sulphur trioxide are taken for one of nitric acid (Expts. No. 17 and 18). Any excess of sulphur trioxide above two molecules (as in Expt. 18) takes no part in the reaction, and is washed out from the products by the nitromethane solvent, as the analytical figures prove.

On the other hand, if nitric acid is supplied in excess of the requirements of the above equation, some of the excess enters into the reaction, and the product consists of a mixture of nitronium hydrogen disulphate and normal nitronium disulphate (Expts. No. 12, 14, 15, and 16). However, even when the nitric acid is furnished in large excess (Expt. 12), we do not obtain the pure normal disulphate, for the reason that this can never be formed from nitric acid and sulphur trioxide, except with the simultaneous production of a protolysing agent, which will bring about a partial reconversion of the normal disulphate into the hydrogen disulphate.

This may be explained for the example in which nitric acid and sulphur trioxide are taken in equimolecular proportions (as in Expts. No. 14, 15, and 16). One then has the correct nitrogen : sulphur ratio for the formation of the normal disulphate. But for every molecule of the normal disulphate produced, one molecule of water must also be formed:

$$2HNO_3 + 2SO_3 = (NO_2^+)_2(S_2O_7^{--}) + H_2O$$

This water is, basically, the protolysing agent. True, it will be immediately converted into other substances, notably sulphuric and disulphuric acids: but this conversion only replaces one proton-donor by another; whether the protolysis of normal nitronium disulphate is a hydrolysis or an acidolysis, its product will be nitronium hydrogen disulphate:

$$(NO_2^+)_2(S_2O_7^{--}) + HB = (NO_2^+)(HS_2O_7^-) + NO_2B$$

When we take nitric acid in substantially larger molecular proportion than the sulphur trioxide (as in Expt. No. 12), we still do not avoid the production of one molecule of water for every molecule of the normal disulphate, in accordance with the above equation. Indeed, we produce the same proportion as before of the basic protolysing agent; and, even though its fate may not now be quite the same in detail, it seems reasonable to expect, as in fact we find (cf. the nitrogen percentages in Table II), a similar amount of protolysis of the normal disulphate.

From the above analysis of the results of Table II, it will be clear that, in order to prepare normal nitronium disulphate in a pure form, it is essential to allow no opportunity for its ready protolysis to the hydrogen disulphate; and therefore it is necessary to conduct the preparation in completely aprotic conditions. This is done in the series of experiments next to be described.

The ionic constitution $(NO_2^+)(HS_2O_7^-)$, of crystalline nitronium hydrogen disulphate has been established by Dr. D. J. Millen (*J.*, 1950, paper no. 509). He has found in the Raman spectrum of the solid substance the characteristic lines of the nitronium and hydrogen disulphate ions; and he has observed no lines foreign to the Raman spectra of these two ions.

Nitronium hydrogen disulphate was obtained from Expts. No. 17 and 18 as a colourless, finely granular precipitate. It had no appreciable vapour pressure at room temperature. In a sealed tube, it melted in the range 100—105°, without obvious decomposition, to a colourless liquid. The precipitated salt recrystallised from warm nitromethane in slender needles, too slender, unfortunately, for *X*-ray analysis by single-crystal methods. Nitronium hydrogen disulphate is extremely hygroscopic, the crystals becoming coated with acid immediately on exposure to the atmosphere. The salt dissolves in water with considerable development of heat, forming a solution of nitric and sulphuric acids. The mixtures of hydrogen disulphate and normal disulphate obtained from Expts. No. 12, 14, 15, and 16 behaved similarly towards water.

(3.4) *Reaction between Dinitrogen Pentoxide and Sulphur Trioxide.—Preparation of nitronium disulphate.* The interaction of these substances was investigated in nitromethane solution. At first the manipulative technique employed was that previously used for the study of the reaction between nitric acid and sulphur trioxide. But for the final experiments of each of two series, a special technique was employed, as will be described below.

Sulphur trioxide is plentifully soluble in nitromethane at temperatures just above the freezing point of the latter, −29°; but the solubility of dinitrogen pentoxide in this solvent is somewhat small at such temperatures. The solutions of dinitrogen pentoxide therefore had to be prepared near 0°; and they then had to be used at once, in order to anticipate the thermal decomposition of the pentoxide, the rate of which is appreciable at temperatures above 0°. As soon as the dinitrogen pentoxide had dissolved, its solution was added to the well-cooled solution of sulphur trioxide. Probably the mixing temperature was between −10° and −5°. In all cases a colourless, crystalline precipitate was immediately formed, which was filtered off, washed, and dried for some days in a good vacuum.

The proportions in which the reactants were brought together, and all the analytical results, are noted in Table III. Of the experiments of the Series I, Nos. 19—22 were carried out with our usual technique. The results show that when not more than two molecular proportions of sulphur trioxide are available to react with one of dinitrogen pentoxide, the precipitated product has, at least approximately, the composition of normal nitronium disulphate, $(NO_2)_2(S_2O_7)$. However, these analytical data are not accurate; and we assumed that this is caused by employment of a technique, which, for the preparation of a substance so extremely sensitive to protolysis, was insufficiently rigorous in excluding the entry of traces of acids with the oxides.

Therefore Expt. No. 23 was conducted in an apparatus in which the dinitrogen pentoxide and sulphur trioxide could be sublimed into separate portions of the solvent, and then, by simply tilting the apparatus, the two solutions could be mixed in the space immediately above the filter-plate. This method should give no opportunity for the entry of acids, and in fact the resulting analyses showed that the normal nitronium disulphate had now been produced in a pure form.

The ionic constitution $(NO_2^+)_2(S_2O_7^{--})$, of crystalline nitronium disulphate has been established by Dr. D. J. Millen (*J.*, 1950, paper no. 509), who found the Raman spectrum of the solid substance to contain the characteristic lines of the nitronium and normal disulphate ions but no lines foreign to the Raman spectra of these two ions.

Nitronium disulphate was obtained in these experiments as small, colourless crystals, without appreciable vapour pressure at the ordinary temperature. Heated in a sealed tube, it decomposed between 100° and 150°, and, near the latter temperature, melted, with a rapid

evolution of brown fumes. The compound is sparingly soluble in nitromethane. It is extremely hygroscopic, the crystals becoming covered with acid immediately on exposure to the atmosphere. It dissolves in water with a large evolution of heat, forming a solution of nitric and sulphuric acids.

TABLE III.

Analysis of products formed from dinitrogen pentoxide and sulphur trioxide.

		AEW.*	N, %.	S, %.
Required values	$(NO_2^+)(HS_2O_7^-)$	44·6	6·27	28·7
	$N_2O_5.2SO_3 = (NO^+)_2(S_2O_7^{--})$	44·7	10·45	23·9
	$N_2O_5.3SO_3 = (NO_2^+)_2(S_3O_{10}^{--})$	43·5	8·04	27·6
	$N_2O_5.4SO_3$ (Pictet and Karl)	42·8	6·54	29·9

	Expt. no.	Reactants.	Analytical results. AEW.*	N, %.	S, %.
Series 1	19	$N_2O_5 + 2SO_3$	44·8	10·28	—
	20	$N_2O_5 + 1·6SO_3$	44·7	9·83	—
	21	$N_2O_5 + 2SO_3$	44·8	10·10	—
	22	$N_2O_5 + 1·6SO_3$	44·5	9·69	—
	23†	$N_2O_5 + 1·6SO_3$	45·0	10·36	24·2
Series 2	24	$N_2O_5 + 4SO_3$	43·8	7·89	—
	25†	$N_2O_5 + 4·8SO_3$	43·8	8·00	—

* AEW = Acid equivalent weight. † Special acid-excluding apparatus used.

(3.5) *Reaction between Dinitrogen Pentoxide and Excess of Sulphur Trioxide.—Preparation of nitronium trisulphate.* It was recalled in Section 2.2 that Pictet and Karl claimed to have obtained a compound of the composition $N_2O_5.4SO_3$, both as the precipitated product of the interaction of dinitrogen pentoxide and sulphur trioxide in solution in carbon tetrachloride, and also as the distilled product of reaction between the two oxides in the absence of a solvent. The preparation of the substance by a process involving distillation at 220° argues very considerable stability. We have attempted to prepare this substance, with results which are summarised in the experiments of Series 2, as reported in Table III.

Exp. No. 24 was an attempt to prepare the compound by bringing together the two oxides in the correct proportions in solution in nitromethane. The analytical results show that the dinitrogen pentoxide has combined with only three molecular proportions of sulphur trioxide.

The attempt was repeated in Exp. No. 25 with two differences in procedure. First, the proportion of sulphur trioxide taken was increased from 4·0 to 4·5 molecules, per molecule of dinitrogen pentoxide, in order to ensure the availability of more than sufficient sulphur trioxide for the formation of Pictet and Karl's compound. This excess should be much more than sufficient to counteract such tendency as could be possessed by a compound, which survives distillation at 220°, to the loss of part of its sulphur trioxide by dissociation under the conditions of its formation at or below the ordinary temperature. Secondly, a special acid-excluding apparatus was used, similar to that employed for Exp. No. 23, in order to obviate any error due to possible protolysis. As appears from Table III, the result of these precautions was to improve the accuracy with which the analytical figures agree with the formula $N_2O_5.3SO_3$: clearly this represents a definite compound.

The structure of this compound, which we call *nitronium trisulphate*, and formulate $(NO_2^+)_2(S_3O_{10}^{--})$, has not yet been specifically determined; but the formula written has been adopted by analogy with nitronium disulphate, and in the light of our recently acquired knowledge concerning the higher polysulphuric acids (Gillespie, *J.*, 1950, 2516; Millen, *J.*, 1950, paper no. 507).

Nitronium trisulphate was obtained in these experiments as a colourless, minutely crystalline substance. It has no appreciable vapour pressure at the ordinary temperature. On heating in a sealed tube, it softens at 105°, and melts below 150° to a colourless liquid, which at about 200° boils without obvious decomposition, and on cooling sets to a colourless solid. It is sparingly soluble in nitromethane. It is extremely hygroscopic. It dissolves in water with a large development of heat, forming a solution of nitric and sulphuric acids.

(3.6) *Stability of Nitronium Hydrogen Sulphate.*—Even though we know from cryoscopic and spectroscopic investigations (*J.*, 1950, 2504 and paper no. 506) that nitronium hydrogen sulphate, $(NO_2^+)(HSO_4^-)$, can exist, and can even be produced quantitatively in solution in sulphuric acid, we have at no time in the course of the present experiments encountered the substance

in crystalline form. As was noted in Section 3.1, Dodé probably obtained it in an impure form. It may be too easily soluble in nitromethane to be crystallised under our conditions. But we think that the main reason why we have not been able to prepare the pure substance is because, in highly concentrated solution, or as solid, indeed, in all condensed forms, the two ions interact fairly rapidly to give the hydrogen disulphate ion and nitric acid:

$$NO_2^+ + 2HSO_4^- = HS_2O_7^- + HNO_3$$

Our procedures of isolation and purification have always been slow enough to allow considerable opportunity for the occurrence of such a reaction; and the tendency of nitronium hydrogen disulphate to be precipitated from nitromethane would encourage such a reaction to proceed to completion. Certainly, nitronium hydrogen disulphate is a main product under all the conditions in which we might expect to obtain nitronium hydrogen sulphate.

As Millen indicates (*J.*, 1950, paper no. 507), this assumed reaction finds spectroscopic support. He notes that, if, to a moderately dilute oleum, as much nitric acid is added as could destroy all the "free" sulphur trioxide (*i.e.*, that which, with sulphuric acid, composes the oleum) according to the equation

$$HNO_3 + SO_3 = NO_2^+ + HSO_4^-$$

then, as the Raman spectrum shows, practically the only dissolved species are, as this equation indicates, the nitronium ion and the hydrogen sulphate ion; but that, if the same experiment is done starting with a highly concentrated oleum, again with an amount of added nitric acid just sufficient to destroy the whole of the "free" sulphur trioxide according to the above equation, then the Raman spectrum shows that comparable amounts of the hydrogen sulphate and hydrogen disulphate ions are present side by side.

In Section 3.1 we described the conversion of nitronium hydrogen sulphate into nitronium hydrogen disulphate as a dehydration of the anion of the former salt by its own cation. Partly in order to cover a case with which we shall meet in Section 4.2, it is convenient to describe the present reaction from a somewhat more general point of view. One may see in it a second limitation to the types of anion with which one may hope to produce crystalline nitronium salts. We noted in Section 1.2 that such anions, in order that they could survive in the presence of nitronium ions, would have to be anions of very strong acids, *i.e.*, they would have to have such a low nucleophilic reactivity as would render them unresponsive towards the high electrophilic reactivity exhibited by the nitronium ion. Now we are reminded that the nitronium ion will even be able to destroy an anion of too low nucleophilic reactivity to participitate in direct combination, if it can break off from such an anion a simpler anion of considerably higher nucleophilic reactivity. Evidently that is what is happening in the reaction under discussion: the nitronium ion is extracting from the hydrogen sulphate ion a hydroxide ion, and is combining with the latter to form nitric acid—leaving the sulphur trioxide to combine with another hydrogen sulphate ion.

(4) *The Reaction between Dinitrogen Pentoxide and Fluorosulphonic Acid: Preparation of Nitronium Fluorosulphonate. The Reaction between Dinitrogen Pentoxide and Chlorosulphonic Acid: Formation of Nitryl Chloride.*

(4.1) *Preparation of Nitronium Fluorosulphonate.*—The reaction between dinitrogen pentoxide and fluorosulphonic acid was conducted in solution in nitromethane by the technique already developed for many of the experiments described in Sections 2 and 3. Equimolecular quantities of dinitrogen pentoxide and of fluorosulphonic acid were dissolved in separate portions of nitromethane at $-10°$, and the solutions were mixed. A crystalline precipitate immediately appeared, which was filtered off, washed, and well dried. The products thus obtained from two such experiments were analysed, with the results shown in Table IV.

These products, when dissolved in water, form fluorosulphonic acid, on the hydrolysis of which to hydrofluoric acid and sulphuric acid the analytical method partly depends. As the errors in the determination of the acid equivalent weight, and of the fluorine content, are rendered appreciable by the low rate of hydrolysis of this substance, a number of control analyses of pure fluorosulphonic acid were made, in order to provide an estimate of the magnitude of the analytical errors. The results of one of these control analyses—a typical one for the standardised procedure employed—are included in Table IV, as an indication of the errors which are discussed in detail in Section 6.3.

TABLE IV.

Analysis of products from dinitrogen pentoxide and fluorosulphonic acid.

Expt. no.	Reactants.		AEW.*	N, %.	F, %.
40	$N_2O_5 + FSO_3H$		36·6	9·6	—
41	$N_2O_5 + FSO_3H$		36·9	9·6	12·8
	Required for $(NO_2^+)(FSO_3^-)$		36·3	9·65	13·1
Control analysis:					
Fluorosulphonic acid		Found	33·7	—	18·7
		Calc.	33·3	—	19·0

* AEW. = Acid equivalent weight after complete hydrolysis.

From these results it is clear that the precipitated salt is pure nitronium fluorosulphonate, $(NO_2^+)(FSO_3^-)$. Its formation from nitrogen pentoxide and fluorosulphonic acid may be represented by the equation

$$N_2O_5 + F{\cdot}SO_3H = (NO_2^+)(F{\cdot}SO_3^-) + HNO_3$$

As Ingold, Millen, and Poole have pointed out (*Nature*, 1946, **158**, 480), crystalline dinitrogen pentoxide is itself nitronium nitrate, $(NO_2^+)(NO_3^-)$. Hence the equation given above may be taken essentially to represent a simple ionic exchange.

Millen has shown by his study of the Raman spectrum of *nitronium fluorosulphonate* (*J.*, 1950, paper no. 509) that this substance has the ionic constitution by which it is represented in the above-written formulæ.

Nitronium fluorosulphonate was obtained as a colourless, finely crystalline precipitate. It crystallises from nitromethane, in which it is somewhat sparingly soluble, in small needles. It has no appreciable vapour pressure at the ordinary temperature. When heated in a sealed tube, it melts at 200° with slow decomposition to a pale yellow liquid. The salt is very hygroscopic. It dissolves in excess of water with a considerable evolution of heat, forming, as the immediate products, nitric acid and fluorosulphonic acid, and ultimately, of course, nitric, hydrofluoric, and sulphuric acids.

(4.2) *Stability of Nitronium Chlorosulphonate.—Formation of nitryl chloride.* An attempt to prepare nitronium chlorosulphonate, by the analogous reaction

$$N_2O_5 + Cl{\cdot}SO_3H = (NO_2^+)(Cl{\cdot}SO_3^-) + HNO_3$$

using the same type of technique, led to quite different results. They can be understood if one supposes that nitronium chlorosulphonate is unstable, the nitronium ion taking a chloride ion out of the anion, so that nitryl chloride and sulphur trioxide are formed, the latter undergoing such further reactions with nitric acid and dinitrogen pentoxide as have already been described in Section 3. In addition to these main reactions, there are side-reactions of an oxidation–reduction type (reminiscent of the *aqua regia* reaction) leading to nitrogen dioxide, chlorine, and presumably sulphuric acid.

Dinitrogen pentoxide (1·5 mols.) and chlorosulphonic acid (1 mol.) were dissolved in separate portions of nitromethane at −10°, and the solutions were mixed. A white precipitate was quickly formed, which, after some hours, was collected on a filter. Gases were evolved during these operations, and a further supply of gaseous products was obtained by pumping out the filtrate. They were collected by condensation in suitably cooled traps. Nitrogen dioxide and chlorine were easily identified. The main product, nitryl chloride, was identified as described below.

Nitryl chloride has been a much disputed substance, all the earlier claims for its preparation having been subsequently denied. The one adequate and authentic description of its preparation is that of Schumacher and Springer (*Z. anorg. Chem.*, 1929, **182**, 139; *Z. Elektrochem.*, 1929, **36**, 653), who obtained it by the action of 100% ozone on nitrosyl chloride. They found it to be a colourless substance, having m. p. −145° and b. p. −16°, which with water gave nitric and hydrochloric acids, and when heated above 100° decomposed into nitrogen dioxide and chlorine.

Our nitryl chloride was collected, together with some chlorine, as an almost colourless solid in a trap at −180°, less volatile substances, including dinitrogen tetroxide, having been retained in preceding traps at −80°. The scale of the experiment was too small to allow the nitryl chloride to be purified by fractional distillation, but, after a complete distillation, its identity was established, without removing the chlorine, by the following tests. The solid substance

melted below −110° to a pale yellow liquid, which boiled below −10°. A portion of the vapour was shaken with a little water: the solution contained chlorine, much nitrate ion and chloride ion, but no nitrite ion. Another portion of the vapour was allowed to enter a tube which had been completely evacuated. When a side-arm attached to this tube was locally heated, it became filled with a dark brown vapour, obviously nitrogen dioxide. No air was present in the tube during this experiment. These tests clearly distinguish the substance from nitrosyl chloride, which forms a deep-red liquid having b. p. −6°, with water gives nitrous acid amongst other products, and on thermal decomposition yields only colourless nitric oxide, besides chlorine.

The crystalline substance which had been collected on the filter was shown by analysis to consist of one or more forms of nitronium disulphate. Its acid equivalent weight was 44·7, which is correct for either the normal disulphate or the hydrogen disulphate. A determination of the nitrogen content would have distinguished between these two possibilities, but this was not done. However, since the substance was produced from chlorosulphonic acid, which is a very strong proton donor, it is practically certain that the main substance which was present was the hydrogen disulphate.

The principal series of decompositions can be approximately represented in the following way:

$$N_2O_5 + Cl{\cdot}SO_3H = (NO_2^+)(Cl{\cdot}SO_3^-) + HNO_3 \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$(NO_2^+)(Cl{\cdot}SO_3^-) + HNO_3 = NO_2Cl + (NO_2^+)(HSO_4^-) \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$2(NO_2^+)(HSO_4^-) = (NO_2^+)(HS_2O_7^-) + HNO_3 \quad . \quad . \quad . \quad . \quad . \quad (3)$$

or, collectively,

$$2N_2O_5 + 2Cl{\cdot}SO_3H = 2NO_2Cl + (NO_2^+)(HS_2O_7^-) + HNO_3$$

Stage (1) is essentially an ion exchange, as already discussed for the reaction between dinitrogen pentoxide and fluorosulphonic acid (Section 4.1). Stage (2) represents the extraction by the nitronium ion of the fairly strongly nucleophilic chloride ion from the very weakly nucleophilic chlorosulphonate ion (cf. Section 3.6). This reaction seems to be complete. Stage (3) is the already considered reaction in which the nitronium ion extracts the strongly nucleophilic hydroxide ion from the weakly nucleophilic hydrogen sulphate ion. In some circumstances this is a measurably balanced reaction (cf. Section 3.6), but it will doubtless go to completion in conditions in which the nitronium hydrogen disulphate is precipitated.

The side-reactions of redox type might be roughly expressed by the equation

$$N_2O_5 + 2Cl{\cdot}SO_3H = N_2O_4 + Cl_2 + H_2SO_4$$

Although the necessary development work has not yet been carried out, it is clear that the reactions now described can be made the basis of a method for the preparation of nitryl chloride—a method which has the attraction that it avoids the operation of preparing pure ozone.

(5) *Formation of Nitronium Salts by the Interaction of Dinitrogen Pentoxide with Selenic Acid.*

It has been shown spectroscopically (*J.*, 1950, paper no. 506) that ionised nitronium hydrogen selenate $(NO_2^+)(HSeO_4^-)$ is quite stable in moderately dilute solution in nitric acid and is, indeed, formed quantitatively when selenic acid is dissolved in concentrations up to 12 mols. % in anhydrous nitric acid.

Although we have obtained crystalline nitronium salts derived from selenic acid, we have not yet succeeded in isolating any one such salt of undoubted individuality. The reluctance with which these substances crystallise renders them considerably more difficult to obtain and to purify, than are the analogous nitronium salts derived from sulphuric acid. On the whole, the analytical evidence suggests that a series of difficultly separable nitronium polyselenates exists, possibly of a similar nature to the already discussed series of nitronium polysulphates (Sections 3.3, 3.4, and 3.5).

We may report an experiment which gave a crystalline product. The selenic acid employed was stated to be free from selenious acid, and we could obtain from it no positive test for selenious acid, although, as is commonly known, the available tests for selenious acid in the presence of much selenic acid are not very critical or sensitive. The selenic acid contained 1·4% of water, but the dinitrogen pentoxide with which it was allowed to react was present in excess. Dinitrogen pentoxide (1·5 mols.) and 98·6% selenic acid (1 mol.) were dissolved

in separate portions of nitromethane at 0°. The solutions were mixed, and the mixture was kept at −10° for some hours with frequent agitation, while a colourless salt slowly crystallised. This was collected on a filter plate, and vacuum-dried for five days. The acid equivalent weight was 61·6, and the nitrogen content was 5·34%. The solution of the salt in water contained nitric and selenic acids. We could obtain no good evidence that it contained any selenious acid, but, again, the unsatisfactory nature of the available tests has to be borne in mind. Whilst the observed analytical figures do not point to any one substance or mixture uniquely, they could be given by several mixtures of nitronium di- and tri-selenates, or of one or more of them with nitronium hydrogen selenate.

(6) *Experimental Methods.*

(6.1) *Materials.*—The methods which we have used for the preparation or purification of several of the substances required for this work, *viz.*, nitric acid, dinitrogen pentoxide, and perchloric acid, are described in accompanying papers (*J.*, 1950, 2400, 2452, 2467). The obtained nitric acid and dinitrogen pentoxide were very pure, but the perchloric acid (cf. Redlich, Holt, and Bigeleisen, *J. Amer. Chem. Soc.*, 1944, **66**, 13) gave analytical figures corresponding to 100·6% acid, and must therefore have contained a little dissolved dichlorine heptoxide. These three substances were stored at −80°. The methods of purification used for most of the other substances are standard, and need no description. The selenic acid, as obtained by us by the concentration of an aqueous solution (cf. Gilbertson and King, *J. Amer. Chem. Soc.*, 1956, **58**, 180), was not anhydrous: it had m. p. 50—55°, and gave analytical values corresponding only to 98·6% selenic acid. Fluorosulphonic acid was prepared as recommended by Meyer and Schramm (*Z. anorg. Chem.*, 1932, **206**, 24). It had b. p. 162—163°, and appeared to be very pure. Perchloric acid monohydrate (hydroxonium perchlorate), m. p. 50°, was prepared by adding the correct amount of water to perchloric acid pre-cooled to −80°. The drying and purification of nitromethane gave some difficulty: the method finally adopted was to dry it first with calcium chloride, and then with magnesium perchlorate, and then to fractionate it.

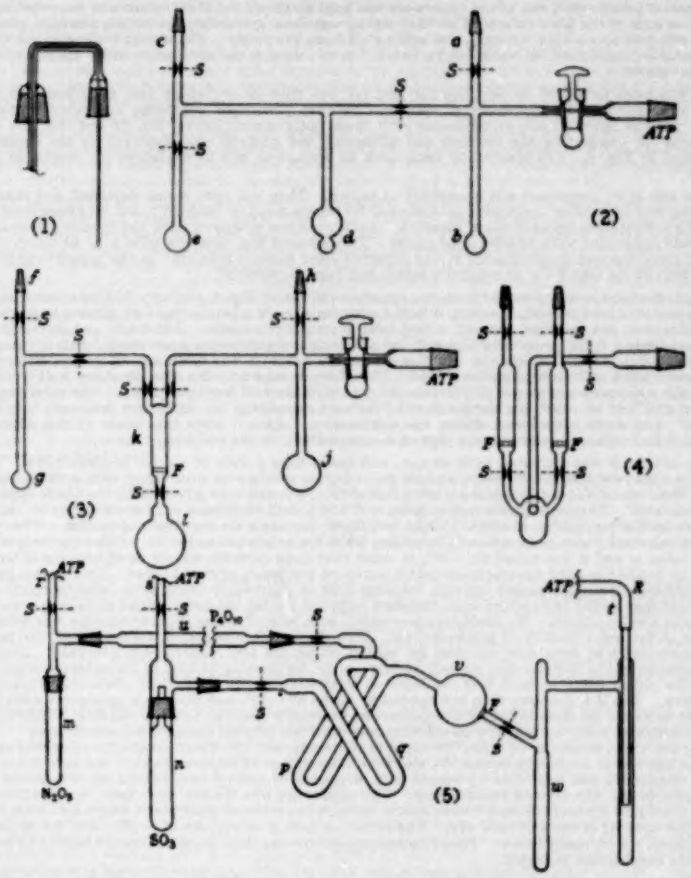
(6.2) *Manipulative Methods.*—Several of the types of apparatus employed are illustrated in Figs. 1—5. Transfers of material from stock were made, when conveniently possible, by non-ebullient distillation at low pressures. When, for liquids or solutions, this was not possible or convenient, any of three other methods of transference was used, each involving a piece of auxilliary apparatus, namely, a capillary funnel, a capillary pipette, and a capillary delivery tube. The last is illustrated in Fig. 1. The funnel worked by gravity, and the pipette by pressure of sulphuric acid in an attached air-reservoir, whilst the delivery tube was brought into operation by the vacuum pump. All ground-glass joints, *e.g.*, those indicated in Fig. 1, were sealed with metaphosphoric acid.

Experiments which did not involve filtration were performed on a simple vacuum line furnished with only bulbs, constrictions *s* for sealing-off, and a single tap, mercury-sealed and lubricated with phosphoric acid, leading to the absorption-tubes, liquid-air trap, and pump *ATP*. An example is illustrated in Fig. 2, which represents the apparatus made for Expt. 5. It was used in the following way. Perchloric acid (*ca.* 1 c.c.) was introduced through joint *a* into bulb *b*, joint *c* being meanwhile closed with a cap sealed on with metaphosphoric acid. Joint *a* was then removed by sealing off at the constriction provided. The apparatus having been evacuated, perchloric acid was transferred by distillation into the double bulb *d*, up to a measured volume given by a mark on the neck between the bulbs. Air was now admitted through the drying tubes to bring the pressure to atmospheric, and then a freshly prepared solution at 0° of dinitrogen pentoxide (3 g.) in nitromethane (15 c.c.) was introduced into bulb *e* through joint *c*. Joint *c* was now removed by sealing off. All the bulbs were now cooled to −80°, while the apparatus was thoroughly pumped out, and the part which contains bulbs *d* and *e* was sealed off from the pump. Bulb *e* was now warmed to −25°, so that the nitromethane melted, and into this solution of dinitrogen pentoxide the perchloric acid was allowed to distil, with occasional gentle shaking. When the transference, and the reaction, were complete, all the volatile material was transferred back into bulb *d* by strongly cooling *d*. The solid reaction product remaining in bulb *e* was dried for one day by maintaining the cooling bath round bulb *d*; and then bulb *e* was sealed off.

As an example of the process of filtration, and of the washing of a precipitate, Expt. 2 may be described. The apparatus made for this experiment is illustrated in Fig. 3. Nitric acid (>1 c.c.) was introduced through joint *f* into bulb *g*, and perchloric acid (*ca.* 12 c.c.) through joint *h* into bulb *j*. The joints *f* and *h* were then sealed off. The bulbs *g* and *j* being strongly cooled, the apparatus was evacuated, and then shut off from the pump by means of the mercury-sealed tap. By cooling to −80° the whole central limb *hl* of the apparatus, up to a point just above the fork, and allowing bulb *g* to become warm, nitric acid could be transferred to the tube *h*, without any of its vapour reaching the perchloric acid in bulb *j*. The nitric acid solidified at the top of tube *h*, but it was caused to melt and run down the tube, and was then resolidified on top of the sintered-glass filter plate *F*. When about 1 c.c. of nitric acid had thus been transferred, the distillation was stopped, and the bulb *g* containing the remainder of the nitric acid was removed by sealing-off. By adjusting the temperature of bulb *j*, about 5 c.c. of perchloric acid were distilled on the layer of solid nitric acid in tube *h*. The nitric acid was allowed to melt, and the two acids to react. Then, by cooling bulb *l* strongly, filtration of the formed precipitate was effected. The remainder of the perchloric acid was then distilled into the tube *h* in three portions, each of which was allowed to mix well with the precipitate before being forced through the filter plate, by reducing the temperature in *l*, and also, if necessary, by admitting a limited amount of dry air through the tap. The bulb *l* being cooled strongly, the apparatus was again completely evacuated; and the precipitate was thus dried in a vacuum for 2 days. It was isolated for analytical purposes by sealing off above and below the tube *h*.

It was found that, in the reactions in which a free acid was used, or could be used, as either reagent, the reaction mixture could, without harm to the product, be allowed to take up the small amount of moisture which is introduced by one transference through air. Thus, in the preparation of nitronium perchlorate from perchloric acid and excess of dinitrogen pentoxide, precautions to exclude every trace of moisture are not essential, and a relatively simple technique will yield a product of purity better than 99%.

FIGS. 1—5.



In such cases, it is mechanically a great convenience to have the apparatus employed for the reaction separate from that used for the filtering, washing, and drying of the reaction product. The separate units of apparatus are then more robust and easily manageable. A filter unit of the seal-off type is illustrated in Fig. 4. It has two filter tubes, between which the reaction product is divided, so that if the contents of one tube are used for analysis there remains in the other a specimen of known composition. A jointed type of filter unit has also been used, which was similar to the unit shown in Fig. 4, except that the four constrictions provided for sealing off were replaced by ground-glass joints, made tight with metaphosphoric acid. Which type of apparatus was used depended on the purpose of the preparation, how long one intended to keep the product, and whether, during a filtration, the solid would easily pass the upper constrictions contained in the seal-off unit.

In illustration of the use of the apparatus shown in Fig. 4, a preparation of nitronium perchlorate by the method of Expt. 8 may be described. Perchloric acid (5 g.) was dissolved in nitromethane (12 c.c.) at −25°. Dinitrogen pentoxide (9 g.) was added to nitromethane (30 c.c.) at −25°, and the mixture was allowed to warm with constant shaking until a clear solution was obtained, which was then immediately mixed with the solution of perchloric acid. The mixture was kept at −20° for 3 hours, in order to allow the crystalline precipitate to become more rapidly filterable, and then it was poured into the filter unit, the upper joints of which were subsequently removed by sealing off. The filtration was effected by operating the pump, while, in order to prevent decomposition, with the formation of nitrosonium perchlorate, the whole apparatus was kept at about −10° by immersion in cooled alcohol up to the tops of the filter tubes. The final drying was done by cooling the filtrate strongly, pumping for several hours to a hard vacuum, and sealing off from the pump. The strong cooling of the filtrate was thereafter continued for several days, before the two filter tubes were removed by sealing off below the filter plates.

As has been indicated in Sections 2.4 and 2.5, the type of technique just described was found to be unsatisfactory for the study of reactions between dinitrogen pentoxide and sulphur trioxide. Hence, for the more critical experiments with these compounds (Expts. No. 23 and 25), the whole apparatus for conducting the reaction and collecting the product was employed as the single unit illustrated in Fig. 5. The method of using such an apparatus will be explained by describing Expt. No. 23.

The well-dried apparatus was assembled as shown. Then the tube *n* was detached and made the receiving end of another apparatus (not shown) by which sulphur trioxide could be transferred from stock by sublimation under reduced pressure. Since very low pressures were not required, the sublimation was conducted with unlubricated joints. This allowed the receiving tube *n* to be fitted with a ground-glass cap and weighed, after it had collected some sulphur trioxide; in the present experiment it was thus found that 2·7 g. of sulphur trioxide had been transferred.

Next, the tube *m* was removed from the apparatus shown in Fig. 5, and attached to another sublimation apparatus (not shown), in which it became the receiver in a transference of dinitrogen pentoxide, by sublimation in a vacuum, through a long tube of phosphoric oxide. The dinitrogen pentoxide was sublimed from a tube, previously charged, by mechanical transference from stock, with the required quantity, 2·3 g., of that substance. In this case a low pressure was used, and all ground-glass joints were made tight with metaphosphoric acid. The charged tube and the receiver being both cooled to −80°, the apparatus was thoroughly evacuated, and then shut off from the pump. The receiving tube *m* being still held at −80°, the temperature of the tube containing the dinitrogen pentoxide was raised to −10°, and there maintained during the sublimation. After 1 hour the whole of the dinitrogen pentoxide had collected, without any sign of decomposition, in the receiving tube *m*.

The U-tube *p* was furnished with 40 c.c., and the U-tube *q* with 30 c.c., of nitromethane. Tubes *m* and *n* were now restored to place, and all ground-glass joints were made good with metaphosphoric acid. Tube *m* and the U-tubes *p* and *q* being cooled to −80°, and tube *n* to −180°, the whole apparatus was evacuated. The three pump connections, *r*, *s*, and *t*, communicated with one another, so that the pressure in the two limbs of either U-tube remained the same during the evacuation. The pump connections *r* and *s* were next removed by sealing off at the constrictions shown. Then the temperature of the tubes *m* and *n* was raised to −10°, in order that their contents should distil into the U-tubes *p* and *q*, on top of the solid nitromethane which occupied the bends of the U-tubes. During this process the dinitrogen pentoxide passed through the long tube of phosphoric oxide *u*, in order to remove any nitric acid that might have arisen from moisture acquired during the last transfer of tube *m* before the apparatus was evacuated. No analogous precaution with respect to the sulphur trioxide was necessary because of the low volatility of sulphuric acid. The empty tubes *m* and *n*, together with the tube of phosphoric oxide *u*, were now removed by sealing off at the two constrictions provided. Next the nitromethane in the U-tubes was melted, at first partly, by pouring alcohol at room temperature over them, the object being to melt first the layer of solid next to the glass, thus obviating breakage by expansion. The U-tubes were then surrounded by baths at −10°, and the whole apparatus was rocked in order to assist the dissolution of the dinitrogen pentoxide and the sulphur trioxide. Through the pump connection *t*, dry air was now admitted slowly until the internal pressure was atmospheric. Then, making use of the flexibility provided by the rubber connexion *t*, the whole apparatus was tilted so that first the solution of dinitrogen pentoxide, and then the solution of sulphur trioxide, ran into the bulb *v*, which meanwhile was kept cool by means of a wrapping of cotton-wool soaked in cold alcohol. A white precipitate was formed immediately. The apparatus was shaken, and then, by operating the pump, the liquid contents of bulb *v* were drawn through the sintered-glass plate, which had been sealed across the opening of the exit tube of *v*. The filtrate in tube *w* was frozen at −180°, and the apparatus was pumped out for many hours. The collected precipitate was then isolated from the filtrate by sealing off at the constriction provided.

(6.3) *Analytical Methods.*—For those analyses which start with the preparation of an aqueous solution, two methods of weighing samples were employed. The samples were usually contained in evacuated sealed filter-tubes, such as form part of the apparatus illustrated in Fig. 4. In the first method, the tube is marked with a file, cleaned, weighed, cracked open, and immersed in water, the parts of the tube being subsequently recovered, washed, dried, and weighed. It was naturally necessary to correct for the absence of air from the tube during the first weighing.

In the cases of the polysulphates, the use of this method was apt to lead to losses by fuming, owing to the large development of heat in the reaction with water. It was found better in these cases, and satisfactory almost always, to cut a filter-vessel open at a narrow extremity, and pour the powdery contents into a tared short tube of the right diameter, standing in a weighing bottle, which could be capped for the weighing. The tube could then be transferred to a stoppered conical flask containing

water, which, however, was allowed to reach the analytical sample only while the ground-glass stopper of the flask was being held firmly in position. Substantially the same method was used in weighing samples for the determination of chlorine by the Carius method.

Except in the case of fluorosulphonates, acid equivalent weights were determined by direct titration of the original solution with carbonate-free 0·05N-sodium hydroxide, methyl-red being the indicator.

Attention was paid to the problem of securing accurate nitrogen determinations by reduction with Devarda's alloy. It is known that when the formed ammonia is distilled through an ordinary Kjeldahl trap, the results tend to be high, partly, it is thought, on account of the carrying of alkaline spray by the ammonia, and perhaps partly owing to the presence of nitride as an impurity in the alloy. Donald (*Analyst*, 1936, **61**, 249) has recommended replacing the Kjeldahl trap by a Davisson trap (*Ind. Eng. Chem.*, 1919, **11**, 465). Vandoni and Chazeau (*Mem. Serv. Chim. de l'Etat*, 1945, **32**, 25) have introduced a new form of trap, and have made other changes in the apparatus. We have tried all three methods, and find that the main difference in the results they produce relates to the magnitudes of blank determinations. Using the quantity of alloy recommended by Donald, we obtained, with the Kjeldahl trap, blank determinations amounting to 1·1—1·2%, with the apparatus of Vandoni and Chazeau, blanks equivalent to 0·8—0·9%, and, with the Davisson trap, blanks corresponding to 0·3—0·4%, of the quantities of nitrate under determination. Therefore our standard procedure involved the use of the Davisson trap, with blank determinations for purposes of correction. Trials with pure sodium nitrate showed that the results obtained in this way were always good to within about 0·3%.

The sulphur in the various nitronium polysulphates was determined as barium sulphate. It is recognised (Allen and Johnston, *J. Amer. Chem. Soc.*, 1910, **32**, 588; Adams and Johnston, *ibid.*, 1911, **33**, 829; Fales and Thompson, *Ind. Eng. Chem. Anal. Eds.*, 1939, **11**, 206) that several partly compensating errors affect the determination of sulphates as barium sulphate; but the error of special concern to us is the known, very marked effect of nitrates in producing high weights of barium sulphate. Using solutions of sulphuric and nitric acid in the proportions in which they would be produced when the different nitronium polysulphates react with water, we found that, under the standard conditions of precipitation used throughout, the presence of nitric acid always raised the weight of the precipitated barium sulphate. For instance, when, along with one equivalent of sulphuric acid, one-third of an equivalent of nitric acid was present, the precipitate was too heavy by 0·5%; and the percentage excess weight appeared to be approximately proportional to the number of equivalents of nitric acid initially present with one of sulphuric acid. On this basis one could apply a correction to the estimated sulphur contents of nitronium polysulphates: it would amount to −0·3% for nitronium hydrogen disulphate, −0·8% for normal nitronium disulphate, and −0·5% for nitronium trisulphate. Such corrections have not actually been applied to the sulphur determination recorded in Tables II and III, but it is clear that, if they were applied, the effect would be considerably to improve the agreement of the results with the calculated values.

Comment is necessary on the analysis of nitronium fluorosulphonate. Nitrogen was determined in the usual way. However, the determination of the acid equivalent weight, and of the fluorine content, involved the problem, which was not fully solved, of securing complete hydrolysis of the fluorosulphonic acid without incurring any loss of the formed hydrofluoric acid. This also applied to the determination of the same quantities for fluorosulphonic acid itself; and therefore the analysis of this substance was studied as a control.

Original solutions, prepared from about 1 g. of nitronium fluorosulphonate, or of fluorosulphonic acid, were made up to 500 c.c. The portions taken for the determination of the acid equivalent weight were first neutralised as usual by titration with standard alkali, methyl-red being the indicator. They were then heated on the water-bath, with neutralisation from time to time by continued titration with standard alkali, until the solution no longer became acid on further heating. The period of heating was about two days. It appears from the examples given in Table IV, that the acid equivalent weights of both nitronium fluorosulphonate and fluorosulphonic acid, as estimated in this way, are about 1·5% too high.

The fluorine in nitronium fluorosulphonate, and also in fluorosulphonic acid, was determined, after total hydrolysis, by precipitating lead fluorochloride along with lead sulphate, and then, after dissolving the precipitate in nitric acid, determining the chloride by potentiometric titration with silver nitrate. A portion (25 c.c.) of the original solution of either substance was diluted to 250 c.c. with water, and the diluted solution was heated for 2 days on the water-bath in order to secure hydrolysis. The fluoride was then precipitated following the standard procedure for the determination of fluoride ion as lead fluorochloride. Lead sulphate, although it is precipitated with the lead fluorochloride, is not precipitated completely enough to give to the weight of the total precipitate any simple analytical significance. Therefore the precipitate was collected in a sintered-glass crucible and washed; and the crucible and its contents were warmed with 1·3N-nitric acid (100 c.c.) until the precipitate had completely dissolved. The solution was then left to cool, and the next day was titrated with 0·012N-silver nitrate. As appears from the examples in Table IV, the results tended to be about 2% low.

Nitrous acid was determined by iodometric measurement of its reducing action on acid permanganate.

We thank Imperial Chemical Industries Limited for help with the cost of this investigation.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, December 17th*, 1949.]

506. *Vibrational Spectra of Ionic Forms of Oxides and Oxy-acids of Nitrogen. Part I. Raman-spectral Evidence of the Ionisation of Nitric Acid by Perchloric, Sulphuric, and Selenic Acids. Spectroscopic Identification of the Nitronium Ion,* NO_2^+.

By C. K. Ingold, D. J. Millen, and H. G. Poole.

This paper extends the account given by Chédin and others of the two Raman lines, 1400 and 1050 cm.$^{-1}$, which are present, but weak, in the spectrum of nitric acid, are intensified strongly, at the expense of molecular nitric acid frequencies, on the addition of sulphuric acid, or dinitrogen pentoxide, or phosphoric oxide, are repressed again, with restoration of nitric acid frequencies, by the subsequent addition of water, and constitute the sole observed spectrum of solid dinitrogen pentoxide. Hitherto the frequency 1400 cm.$^{-1}$ has always been accompanied by 1050 cm.$^{-1}$, the two being comparable in intensity over a great range of intensities. The frequency 1400 cm.$^{-1}$ has now been developed without its companion by the addition to nitric acid of either perchloric acid or selenic acid. This shows that the two lines do not come from a common molecular source, and a detailed study of the spectra proves that the source of the frequency 1400 cm.$^{-1}$ has no other line in its spectrum. The source is thus unambiguously identified as the nitronium ion: no other structure, which could be composed from the elements in nitric acid, would yield the observed spectral characters.

The source of the companion frequency 1050 cm.$^{-1}$, as produced by the use of sulphuric acid, has several other lines in its Raman spectrum: they are shown to belong to, and to identify, the hydrogen sulphate ion. When the frequency 1400 cm.$^{-1}$ is developed by the use of perchloric acid, other Raman lines appear: they belong to, and they identify, the perchlorate ion. When the frequency 1400 cm.$^{-1}$ is developed with the aid of selenic acid, still other lines appear: they belong to, and identify, the hydrogen selenate ion. Generally, every spectral appearance, which could be expected from the following assumed modes of ionisation of nitric acid, is observed:

$$HNO_3 + 2H_2SO_4 = NO_2^+ + H_3O^+ + 2HSO_4^-$$
$$HNO_3 + 2HClO_4 = NO_2^+ + H_3O^+ + 2ClO_4^-$$
$$HNO_3 + 2H_2SeO_4 = NO_2^+ + H_3O^+ + 2HSeO_4^-$$

In the example of ionisation in sulphuric acid, the reversibility of the process is demonstrated, again in extension of Chédin's work. He showed that nitric acid lines, which had been weakened by the addition of sulphuric acid, could be restored by adding water; and it is now shown that they can also be restored by adding potassium hydrogen sulphate. The significance of the other known appearances or intensifications of the frequencies 1400 and 1050 cm.$^{-1}$ is treated in Part V (*J.*, 1950, paper no. 510).

(1) *Objects and Methods.*

(1.1) *Object of this Series of Papers.*—The aim of the work to be described in the papers of this series is the spectroscopic study of the ionic forms assumed by nitric acid, by nitrous acid, and by the related oxides of nitrogen, not only in solution in various types of solvents, but also in the crystalline lattices of salt-like compounds.

The manner in which this problem originally presented itself in connexion with an investigation of the kinetics and mechanism of aromatic nitration is described in an accompanying paper by Hughes, Ingold, and Reed (*J.*, 1950, 2400). The place of the present investigation in the subsequently planned, general study, by the available physical methods, of ionisation phenomena in very strongly acidic solvents such as sulphuric acid, follows fairly obviously from the historical outline of this subject which is given in another of the accompanying papers (Gillespie, Hughes, and Ingold, *J.*, 1950, 2473).

(1.2) *Object of the Present Paper.*—This first paper of the present series deals with the ionisation of nitric acid in three very strongly acidic solvents. The development of this limited section of the wider field of ionisation in such solvents is outlined in yet another of the accompanying papers (Gillespie, Graham, Hughes, Ingold, and Peeling, *J.*, 1950, 2504).

The technique now employed is that of Raman spectroscopy. The three statements to which reference has been made being conveniently available, all we shall have to do, in order to complete the account of the background on which the present work was laid, will be to summarise the results which have been obtained by application of the Raman-spectroscopic technique to our problem. This is done in Section 2.1.

The principal outcome of the work described in this paper has already been reported in summary (*Nature*, 1946, **158**, 480).

(1.3) *Experimental Arrangements.*—The main parts of the apparatus, including the spectrograph and the microphotometer, and the general methods of recording and evaluating spectra, were the same

as those which Poole had employed (cf. *J.*, **1946**, 245) for the study of the deuterated benzenes, except for modifications necessitated by the different nature of the material now under examination. Such material falls into several classes, each requiring a different experimental arrangement.

One such class consists of liquids which are available in quantity and are not decomposed by the exciting radiation. This class includes sulphuric acid, aqueous sulphuric acid, mixtures of nitric and sulphuric acids containing less than about 80% of nitric acid, and dilute solutions of dinitrogen pentoxide, tetroxide, and trioxide, in sulphuric acid. The cell used for these liquids consisted of a Pyrex tube, 40 cm. long and 2 cm. in diameter, which contained two optical windows 36 cm. apart. These were fixed by shrinking the tube on to them in the blowpipe, and then carefully annealing the whole. The cell was mounted co-axially with the collimator, and a lens was interposed which focused the centre of the more remote window on the slit of the spectrograph. The contents of the cell were illuminated by means of two low-pressure, direct-current, quartz, mercury arcs, about 45 cm. long, each carrying a current of 3·5 amps.

Anhydrous nitric acid and many of its solutions constitute another class of liquid which includes those mixtures of nitric acid with perchloric acid, or sulphuric acid, or selenic acid which contain more than about 80% of nitric acid. Observation of the Raman spectra of these liquids is rendered difficult by decomposition, resulting in a yellow material which absorbs practically all the Raman radiation excited by the mercury lines 4047 A. and 4358 A. The decomposition is accelerated by the shorter-wave light from the mercury arc, but is retarded by a reduction of temperature. In order to obtain spectra of satisfactory intensity, it was found desirable to maintain the cell contents below −10°, and to employ Hg 4358 A. for the excitation, the other violet line, Hg 4047 A., and the ultra-violet part of the mercury spectrum, being filtered out as completely as possible. The cell was like that described above, except that it was only 10 cm. long and was jacketed. Through the jacket a cooled solution of *m*-dinitrobenzene and rhodamine in alcohol was pumped, which maintained the cell contents at about −15°, and removed the more photochemically active light, thus permitting useful exposures up to about 16 hours. The local heating produced by the arcs was sufficient to keep the outer wall of the cooling jacket free from ice. The cell window nearest to the spectrograph was kept clear by passing a stream of warm, dry air across it.

Liquids available in rather smaller quantity, for instance, solutions of certain sulphates, or disulphates in oleum, were treated by the Wood's-tube method (cf. Poole, *loc. cit.*).

Crystalline solids, such as nitronium salts, were examined as powders, a special system of filters being employed in order to reduce the continuous spectral background and the otherwise excessive amount of light reflected into the spectrograph from the crystal surfaces. The cell consisted of a short Pyrex tube with a window sealed-in near the centre, and a male ground joint at one end. The solid was pressed against the window to form a pellet of depth about 0·5 cm., and the tube was then closed by means of a ground cap, sealed on with metaphosphoric acid. The cell was mounted on the axis of the collimator, and a lens was used in order to focus the Raman radiation on the slit. The light from the lamps passed through concentric, annular, praseodymium and cobalt filters (cf. Poole, *loc. cit.*), arranged co-axially with the cell, and the Raman radiation, on its way to the spectrograph, passed through an *o*-nitrophenol filter, in order to remove some of the surface-reflected light. It was found important to keep the arcs cool by means of an air blast, not only for the purpose of reducing the spectral background, but also in order that they could be placed quite close to the cell, thus increasing the intensity of the irradiation and reducing the needed exposure. The weakest of the perchlorate ion fundamentals, usually described as a diffuse band (cf., however, Part IV), could thus be obtained satisfactorily from powdered perchlorate with an exposure of 70 hours.

(1.4) *Preparation of Materials.*—The methods used for the preparation of most of the materials required for this work are described in accompanying papers (*J.*, 1950, 2400, 2452, 2504, 2559). This applies, in particular, to nitric acid (cf. *J.*, 1950, 2400), but the preparation of the other strong acids requires some description here.

The sulphuric acid used was essentially 100% acid supplied by British Drug Houses Ltd.; but, before use, it was heated at 100° for 2—3 hours, in order to secure destruction of a trace of some impurity which caused a troublesome fluorescence under the conditions of excitation of the Raman spectra.

Anhydrous perchloric acid was prepared from 60% acid by distillation from excess of sulphuric acid in an apparatus similar to that used for the preparation of anhydrous nitric acid.

Anhydrous selenic acid was obtained from commercial 92% acid by crystallisation. It was collected by filtration in a stream of dry air, and kept in a vacuum over phosphoric oxide.

Oleum was prepared by redistilling freshly distilled sulphur trioxide under reduced pressure on to solid sulphuric acid at −80°, and allowing the mixture to warm to room temperature. The composition having been controlled by weighing, the oleum was diluted suitably by the addition of 100% sulphuric acid. The diluted oleum was heated at 100° for 2—3 hours in order to destroy sources of fluorescence.

(2) *The Cation in Solutions of Nitric Acid in Very Strong Acids.*

(2.1) *Some Non-mixture-law Lines in the Raman Spectra of Mixtures of Nitric and Sulphuric Acids.*—The intense and very sharp line of frequency 1400 cm.$^{-1}$, which the Raman spectra of these mixtures always contain, and which obviously does not belong either to the nitric acid or to the sulphuric acid molecule, was first recorded by Médard (*Compt. rend.*, 1934, **199**, 1615). A similar line was found in the Raman spectrum of a solution of dinitrogen pentoxide in nitric acid by Briner and Susz (*Helv. Chim. Acta*, 1935, **18**, 378). A weak line of the same frequency was reported by Angus and Leckie in the Raman spectrum of anhydrous nitric acid (*Proc. Roy. Soc.*,

1935, *A*, **149**, 327); but they did not identify it with Médard's line. However, Chédin definitely recognised the weak appearance of Médard's frequency in the spectrum of anhydrous nitric acid; and most of our information about this frequency is due to Chédin (*Compt. rend.*, 1935, **200**, 1397; 1935, **201**, 552, 714; 1936, **202**, 220, 1067; 1936, **203**, 772, 1509; *Ann. Chim.*, 1937, **8**, 243). This Raman line is not only very sharp; it is also highly polarised. Chédin's value for its depolarisation factor is $\rho = 0{\cdot}19$, and an almost identical figure has been recorded by Venkateswaran (*Proc. Indian Acad. Sci.*, 1936, *A*, **4**, 174).

The discovery of Médard's frequency in anhydrous nitric acid showed that the source of the frequency must be some product of a self-reaction of nitric acid. Chédin proved in detail that the frequency is associated with the product of a dehydration of nitric acid. He showed, for instance, that if successive amounts of sulphuric acid are added to nitric acid, the frequency 1400 cm.$^{-1}$ will reach a maximum of intensity, while simultaneously the lines of the nitric acid molecule will weaken and finally disappear; and that if, when this has happened, some water is added, it will reduce the intensity of the frequency 1400 cm.$^{-1}$, and at the same time bring back the lines of the nitric acid molecule. Consistently with Briner and Susz's observation, Chédin showed that the frequency 1400 cm.$^{-1}$ of anhydrous nitric acid becomes greatly intensified in solutions of dinitrogen pentoxide in nitric acid, or in anhydrous acid to which phosphoric oxide has been added.

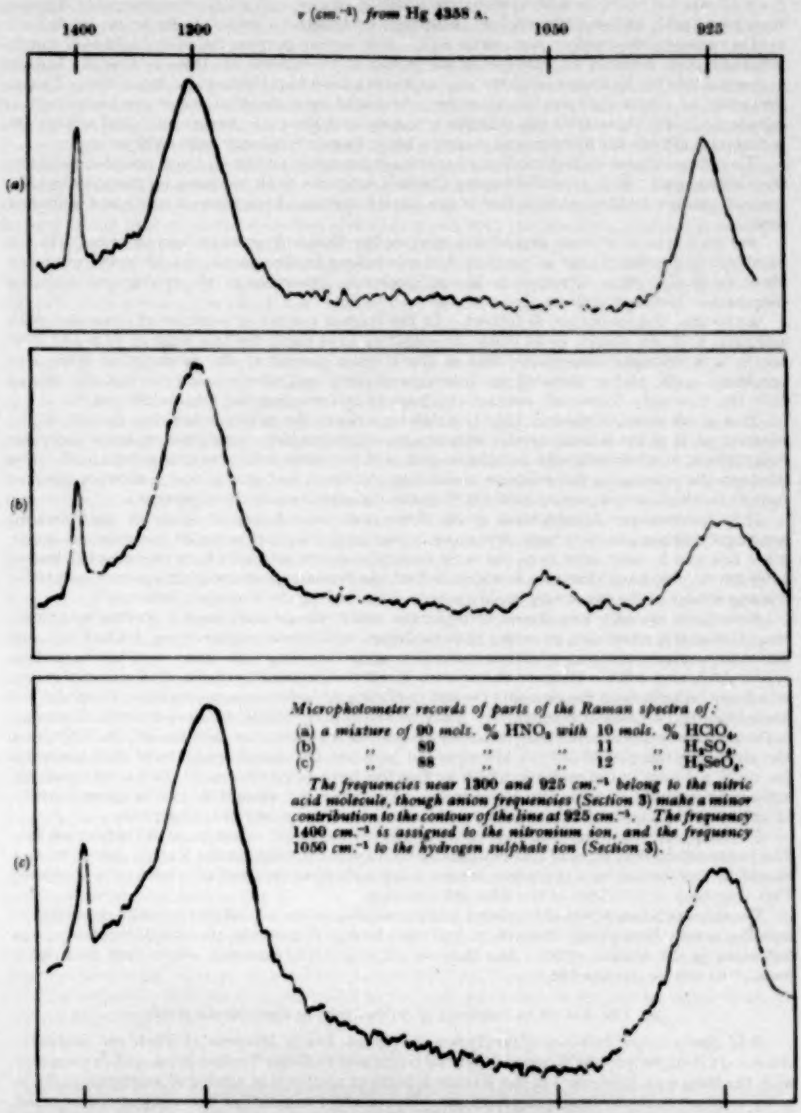
Throughout the above work it was noticed that a second non-mixture-law Raman line, having the frequency of about 1050 cm.$^{-1}$, appeared to be closely associated with the frequency 1400 cm.$^{-1}$. All investigators have found that whenever the frequency 1400 cm.$^{-1}$ occurred, the frequency 1050 cm.$^{-1}$ occurred also, the two always remaining comparable in intensity over a great range of intensities. Thus, as Angus and Leckie and also Chédin found, both lines occur weakly in the spectrum of anhydrous nitric acid. As Briner and Susz and also Chédin observed, both lines are strongly developed in the spectra of solutions of dinitrogen pentoxide in nitric acid; and likewise, as Chédin found, in the spectrum of nitric acid treated with phosphoric oxide. Chédin showed in detail that, as the composition of mixtures of nitric acid and sulphuric acid was changed, the intensities of the two lines varied in a parallel manner. Finally, Chédin found the same two lines, again together, as the sole visible lines in the Raman spectrum of solid dinitrogen pentoxide.

It was an obvious conclusion from this evidence that the two frequencies, 1400 and 1050 cm.$^{-1}$, have a common origin. Briner and Susz originally suggested that they belong to dinitrogen pentoxide. Chédin showed, however, that the Raman spectrum of dinitrogen pentoxide in neutral solvents, and, in particular, in a solvent in which it was known from cryoscopic observations to have a normal molecular weight, is entirely different. He therefore assumed the two frequencies to arise, not from the normal molecule of dinitrogen pentoxide, but from a special form of that substance. Bennett, Brand, and Williams interpreted these results and conclusions on the basis that Chédin's special form is the ionised form (*J.*, 1946, 869). In particular, they assigned the frequency 1400 cm.$^{-1}$ to the nitronium ion, comparison with the isoelectronic molecule carbon dioxide having shown that a polarised Raman frequency would be expected in this region. They attributed the frequency 1050 cm.$^{-1}$ to the nitrate ion, or, in the presence of sulphuric acid, to the hydrogen sulphate ion, assignments which are consistent with the known spectra of these anions. In the following Sections we shall supply spectroscopic demonstrations of the correctness of these interpretations.

(2.2) *Some Non-mixture-law Lines in the Raman Spectra of Mixtures of Nitric Acid with Perchloric Acid and with Selenic Acid.*—The basis of the method now employed in order to establish the origin of the frequency 1400 cm.$^{-1}$ may be explained as follows. Invariably hitherto, the Raman line at 1400 cm.$^{-1}$ has appeared in company with the line at about 1050 cm.$^{-1}$, the two having such intensity relations as would indicate a common molecular source. But spectroscopic theory shows that if two such lines should arise from a common source, then that source could not be anything as simple as the nitronium ion, which belongs to the very limited class of molecules that cannot have more than one strong Raman line. We are allowed to assume that the frequency 1400 cm.$^{-1}$ belongs to the nitronium ion, if we suppose that the frequency 1050 cm.$^{-1}$ arises from some second source, such as an associated anion, which, for stoicheiometric reasons, is always formed along with, and in quantity equivalent to, the nitronium ion. However, the simplest way to establish this theory, and, indeed, to prove that the source of the frequency 1400 cm.$^{-1}$ has one, and not two, strong lines in its Raman spectrum, would be to isolate the frequency 1400 cm.$^{-1}$ from its hitherto constant companion.

The conditions required for doing this are readily predicted. In the first place, the nitrate ion is known to have a strong Raman frequency at about 1050 cm.$^{-1}$, and therefore any nitrate

FIG. 1.



Microphotometer records of parts of the Raman spectra of:

(a) *a mixture of* 90 *mols.* % HNO_3 *with* 10 *mols.* % $HClO_4$.
(b) ,, 89 ,, ,, 11 ,, H_2SO_4.
(c) ,, 88 ,, ,, 12 ,, H_2SeO_4.

The frequencies near 1300 *and* 925 *cm.*$^{-1}$ *belong to the nitric acid molecule, though anion frequencies (Section* 3*) make a minor contribution to the contour of the line at* 925 *cm.*$^{-1}$. *The frequency* 1400 *cm.*$^{-1}$ *is assigned to the nitronium ion, and the frequency* 1050 *cm.*$^{-1}$ *to the hydrogen sulphate ion (Section* 3*).*

ion which is, or might be, present in nitric acid, or a mixture containing it, must be excluded. Such nitrate ion could be destroyed by the addition of any acid which is considerably stronger than nitric acid, and would therefore quantitatively transfer a proton to its anion. Sulphuric acid is considerably stronger than nitric acid. But for our purpose the added acid may not be sulphuric acid, because, in transferring its proton to the nitrate ion, this acid would become converted into the hydrogen sulphate ion; and it is known that this ion also has a strong Raman frequency at about 1050 cm.$^{-1}$. However, the added acid could be either perchloric acid or selenic acid; for these acids are sufficiently strong to destroy the nitrate ion; and neither the perchlorate ion nor the hydrogen selenate ion has a Raman frequency near 1050 cm.$^{-1}$.

Therefore we have studied the Raman spectra of mixtures of nitric acid with perchloric acid and with selenic acid; and, notwithstanding Chédin's extensive work, we have, for purposes of comparison, made a further examination of the Raman spectra of mixtures of nitric and sulphuric acids.

For each type of mixture several non-mixture-law Raman lines have been observed. It will be shown in Section 3 that all of them but one belong to the anions present in the mixtures. Here we shall confine attention to the occurrence or otherwise of the two non-mixture-law frequencies, 1400 and 1050 cm.$^{-1}$.

As to this, the results are as follows. In the Raman spectra of mixtures of nitric acid with sulphuric acid, we obtain, as all other investigators have done, the two lines at 1400 and 1050 cm.$^{-1}$, both strongly developed. But in the Raman spectra of the mixtures of nitric and perchloric acids, and in those of the mixtures of nitric and selenic acids, we find the line at 1400 cm.$^{-1}$ strongly developed, without any trace of an accompanying line at 1050 cm.$^{-1}$.

This result is established in Fig. 1, which reproduces the microphotometric records of the relevant parts of the Raman spectra of mixtures, approximately corresponding as to molecular composition, of nitric acid with perchloric acid, with sulphuric acid, and with selenic acid. The photographs relating to the mixtures containing perchloric and selenic acid constitute the first records in which the frequency 1400 cm.$^{-1}$ stands isolated from its usual partner.

(2.3) *Spectroscopic Identification of the Nitronium Ion.*—A careful study of such Raman spectra of mixtures as have been illustrated in Section 2.2 has not revealed the presence of any other line which could arise from the same molecular source as that which produces the line at 1400 cm.$^{-1}$. We have therefore to conclude that the Raman spectrum of this source essentially consists simply of the one strong, highly polarised line having the frequency 1400 cm.$^{-1}$.

Now there are only two classes of molecules which should have such a Raman spectrum, *viz.*, (1) diatomic molecules, including both the homo- and hetero-nuclear types, AA and AB, and (2) linear, centrosymmetric, triatomic molecules, again including both homo- and hetero-nuclear types, AAA and ABA. Because the spectra of all the chemically stable, diatomic molecules, which can be built from the elements present in nitric acid, are known, all diatomic molecules are excluded from the present assignment. Only two chemically stable, centrosymmetric, triatomic molecules can be constructed from the elements in nitric acid, *viz.*, the azide ion $(N{=}N{=}N)^-$, and the nitronium ion $(O{=}N{=}O)^+$. We need not here use the chemical argument that the azide ion could not exist in the media in which we find the frequency 1400 cm.$^{-1}$: its known spectrum suffices to exclude it from the assignment. And thus the nitronium ion is unequivocally identified as the source of the frequency 1400 cm.$^{-1}$ on purely spectroscopic grounds.

The frequency 1400 cm.$^{-1}$ belongs to the totally symmetrical vibration of the nitronium ion. The fundamental frequency of this vibration should appear strongly in the Raman spectrum, and should be represented by a sharp line, having a depolarisation factor of about 0·2, as is observed. This frequency is forbidden in the infra-red spectrum.

The other two fundamental frequencies of the nitronium ion, *viz.*, the non-totally symmetrical non-degenerate (stretching) frequency, and the doubly degenerate (bending) frequency, are forbidden in the Raman effect. But they are allowed in the infra-red, where they have been found,* as will be reported later.

(3) *The Anions in Solutions of Nitric Acid in Very Strong Acids.*

(3.1) *Spectroscopic Detection of the Hydrogen Sulphate Ion in Mixtures of Nitric and Sulphuric Acids.*—It is implicit in the foregoing that the frequency 1050 cm.$^{-1}$, when developed in company with the frequency 1400 cm.$^{-1}$ in the Raman spectra of mixtures of nitric and sulphuric acids, is to be ascribed to the hydrogen sulphate ion. But in order to establish this assignment we must show that all the spectral appearances which are to be expected from the presence of the hydrogen

* By Mr. H. Cohn, using crystalline nitronium salts.

sulphate ion are to be found in the spectra of the mixtures. This necessitates a somewhat detailed examination of the spectra for the following reasons.

In the first place, sulphuric acid, like nitric acid, gives a fairly rich spectrum of Raman lines; and all the main lines are broad, doubtless on account of the strong intermolecular hydrogen-bonding which occurs in the liquid acid. Then, the majority of hydrogen sulphate ion frequencies must lie quite close to molecular sulphuric acid frequencies. This is to be expected theoretically; for the difference of a proton between the two structures is largely local, affecting mainly one of four similar peripheral masses, and one of four similar radial bonds. Only a few frequencies of the hydrogen sulphate ion, those with much motion of a unique type in the OH-group, can be markedly different from molecular sulphuric acid frequencies. Having regard to the great breadth of the Raman lines of sulphuric acid, it follows that the spectroscopic identification of the hydrogen sulphate ion in the presence of a large excess of sulphuric acid molecules will depend to some extent at least on the detection of heavily overlapped satellite lines, whose presence can be established only by careful study of the microphotometric contours.

According to Woodward and Horner (*Proc. Roy. Soc.*, **1934**, *A*, **144**, 129) and others, the hydrogen sulphate ion is characterised by three Raman frequencies which are observably different from molecular sulphuric acid frequencies: in cm.$^{-1}$ they are as follows:

590 (m) 895 (mw) 1050 (s)

(Here, and later, we use the following contractions as qualitative indications of intensity in Raman spectra: vs = very strong, s = strong, ms = moderately strong, m = medium, mw = moderately weak, w = weak, vw = very weak.)

Of these frequencies, only one occurs in a spectral region almost completely free from molecular sulphuric acid lines. This is the frequency 1050 cm.$^{-1}$, which is much stronger than the others, and is therefore a good index for the hydrogen sulphate ion in sulphuric acid solutions. According to Venkateswaran (*loc. cit.*), this Raman line is considerably polarised. We suppose it to belong to a vibration which essentially involves S–OH stretching, and is rendered markedly different from all molecular sulphuric acid vibrations, and closely similar to what would be a totally symmetrical vibration if the H-atom were on the SO-axis, by accompanying trigonally symmetrical movements of the other three oxygen atoms.

The next of the frequencies of the hydrogen sulphate ion in order of diminishing strength is 590 cm.$^{-1}$; but this lies so close to the fairly strong molecular sulphuric acid frequency 560 cm.$^{-1}$ that it is impossible to resolve them in any known conditions. However, as we shall illustrate below, the presence of the ionic frequency 590 cm.$^{-1}$ as a satellite to the stronger molecular frequency 560 cm.$^{-1}$ can often be seen rather easily as a dissymmetry in the microphotometric contours of the latter.

The third of the hydrogen sulphate frequencies, 895 cm.$^{-1}$, is not only weaker still, but also it lies still closer to the still stronger and broader frequency, 910 cm.$^{-1}$, of molecular sulphuric acid. In this case the observation of the ionic frequency as a satellite to the molecular frequency is by no means easy; but, as we shall illustrate below, it can just be done, in the conditions which are of interest to us, by means of a careful comparison of line thicknesses.

We record in Table I the results of some measurements of the main Raman frequencies of (*a*) anhydrous sulphuric acid, (*b*) a 3M-solution of water in sulphuric acid, and (*c*) a 3M-solution of nitric acid in sulphuric acid. The listed frequencies are Raman displacements of Stokes lines excited by Hg 4358 A., simultaneous excitation by Hg 4047 A. being excluded in the usual manner by means of nitrite filter. The three spectra are reproduced in the form of microphotometer records in Fig. 2.

The most obvious differences between these spectra are that the spectrum of the solution of water contains all the stronger lines of that of the sulphuric acid solvent, together with a line at 1050 cm.$^{-1}$; whilst the spectrum of the solution of nitric acid contains all the stronger lines of that of the solvent, together with the two lines at 1050 cm.$^{-1}$ and 1400 cm.$^{-1}$.

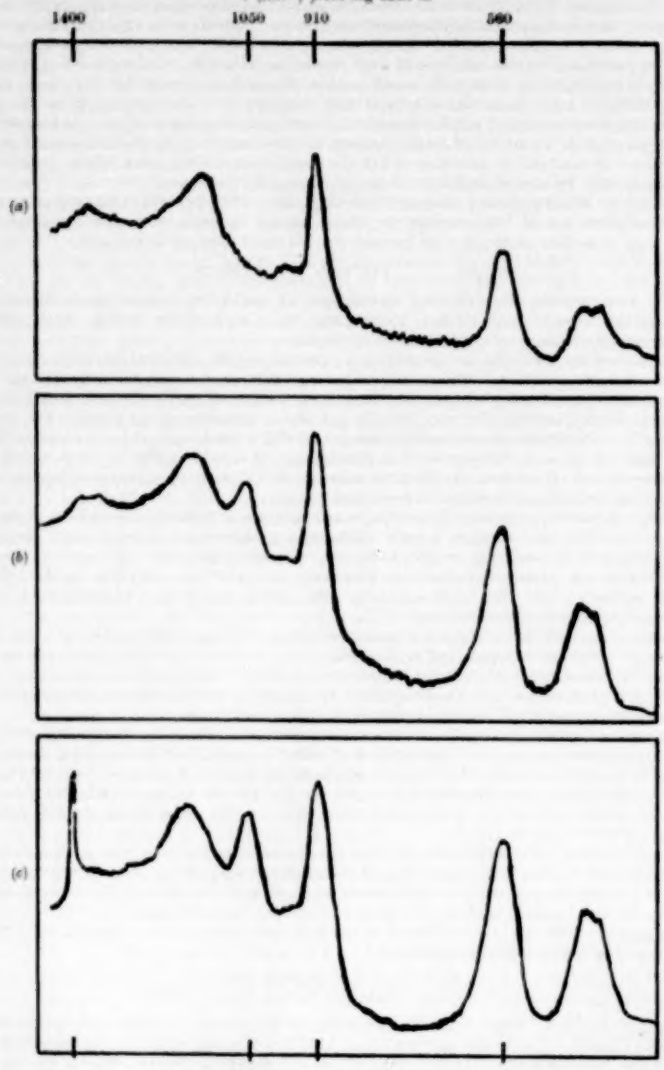
The frequency 1050 cm.$^{-1}$ is attributed to the hydrogen sulphate ion formed in solutions (*b*) and (*c*) according to the following equations:

$$(b)\ H_2O + H_2SO_4 = H_3O^+ + HSO_4^-$$
$$(c)\ HNO_3 + 2H_2SO_4 = H_3O^+ + NO_2^+ + 2HSO_4^-$$

Two points of detail, by which this assignment can be supported, are illustrated in the microphotometric records. The first is that the line at 1050 cm.$^{-1}$ has the same type of contour in both the spectra in which it occurs. It is a recognisably different contour from that of the identical Raman frequency which can be developed from nitric acid by other means than the addition of

FIG. 2.

Microphotometer records of parts of Raman spectra of (a) *anhydrous sulphuric acid,* (b) *a* 3*M*-*solution of water in sulphuric acid, and* (c) *a* 3*M*-*solution of nitric acid in sulphuric acid.*



sulphuric acid, and which can be shown to be due to the nitrate ion (cf. Part V, Figs. 1 and 2, *J.*, 1950, paper no. 510). The other point is that, relatively to the lines of molecular sulphuric acid, the line at 1050 cm.$^{-1}$ is approximately twice as intense in the spectrum of the solution of nitric acid as it is in that of the equimolar solution of water. This is as it should be, according to the above chemical equations, which, however, neglect the incompleteness in the ionisation of water (Gillespie, *J.*, 1950, 2493); but, even when the incompleteness of ionisation is taken into account, the intensity ratio should still be approximately 2 : 1, as is observed.

TABLE I.

Raman frequencies of (a) *sulphuric acid*, (b) *a* 3M*-solution of water in sulphuric acid, and* (c) *a* 3M*-solution of nitric acid in sulphuric acid.*

Solute.	Frequency separation in cm.$^{-1}$ from Hg 4358 A.								
(*a*) None	391 ms	417 ms	562 s	912 s	976 w	—	1125—95 s	1377 mw	—
(*b*) H_2O	393 ms	415 ms	566 s	914 s	—	1050 ms	1150 s	—	—
(*c*) HNO_3	392 ms	418 ms	565 s	911 s	—	1045 ms	1170 s	—	1402 ms

It is easy to see that the hydrogen sulphate ion frequency 590 cm.$^{-1}$ is present, not only in the solution of water, but also in that of nitric acid. This is shown by the dissymmetry and basal breadth of the molecular sulphuric acid line at 560 cm.$^{-1}$ in the spectra of the two solutions. These appearances are more marked in the spectrum of the solution of nitric acid than in that of the solution of water, as they should be.

TABLE II.

Raman frequencies of mixtures of nitric and sulphuric acids.

(Frequency separations in cm.$^{-1}$ from Hg 4358 A.)

Compositions in percentages of nitric acid by volume.

0.	10.	20.	30.	50.	60.	70.	80.	90.	100.
391	392	399	—	—	—	—	—	—	—
ms	m	mw	—	—	—	—	—	—	—
416	417	415	419	422	421	420	428	428	—
ms	ms	m	m	m	m	m	w	vw	—
562	564	565	573	573	574	577	580	585	—
ms	ms	ms	ms	ms	m	m	m	m	—
—	—	—	618	620	621	621	620	615	609
—	—	—	m	ms	ms	ms	ms	ms	ms
—	—	—	681	681	679	679	679	678	677
—	—	—	w	m	ms	ms	ms	ms	ms
912	910	908	904	915	932	935	930	927	925
s	s	s	s	s	vs	vs	vs	s	s
976	—	—	—	—	—	—	—	—	—
w	—	—	—	—	—	—	—	—	—
—	1045	1043	1043	1044	1045	1049	1050	1053	1049
—	ms	s	vs	vs	vs	vs	s	s	w
1125—95	1164	1171	1166	1181	1173	1186	—	—	—
s	s	ms	ms	m	m	mw	—	—	—
—	—	1315	1314	1314	1312	1312	1306	1303	1296
—	—	m	ms	s	vs	vs	vs	vs	vs
1376	—	—	—	—	—	—	—	—	—
w	—	—	—	—	—	—	—	—	—
—	1402·1	1401·4	1400·0	1398·3	1398·0	1398·4	1398·7	1396·3	1392
—	s	s	vs	vs	vs	s	s	s	w
—	—	—	1537	1545	1541	1544	1540	1540	1533
—	—	—	vw	w	w	mw	mw	mw	w
—	—	—	1666	1680	1675	1674	1675	1676	1670
—	—	—	w	mw	m	ms	ms	ms	ms

Even the weak hydrogen sulphate frequency, 895 cm.$^{-1}$, is discernible in the spectra of the two solutions. It can be seen as a slight, but distinct, thickening of the sulphuric acid line at

910 cm.$^{-1}$. Consistently, the thickening is appreciably greater in the spectrum of the solution of nitric acid than it is in that of the solution of water.

Some Raman frequencies, which have been measured in the course of a systematic survey of the Raman spectra of a series of mixtures of nitric and sulphuric acids, covering the whole range of composition of such mixtures, are reported in Table II. These results, which are in general agreement with those of Chédin, provide further confirmation of the presence of the hydrogen sulphate ion in the mixtures.

The main general features which these data illustrate are as follows. The spectrum of pure sulphuric acid contains only molecular sulphuric acid lines.* The spectra of mixtures of the acids made with a sufficiently small proportion of nitric acid, *e.g.*, 10%, contain no molecular nitric acid lines; but they contain molecular sulphuric acid lines, the nitronium ion line at 1400 cm.$^{-1}$, and the hydrogen sulphate ion line at 1050 cm.$^{-1}$, as well as the other appearances, indicative of the presence of weak satellite lines, as have already been attributed to the hydrogen sulphate ion. Let us defer for the moment consideration of the mixtures of intermediate compositions. The spectra of mixtures made with a sufficiently large proportion of nitric acid, *e.g.*, 90%, contain no molecular sulphuric acid lines, or at most only one weak one at 428 cm.$^{-1}$, which might, however, be a weak hydrogen sulphate ion line; instead, these spectra contain molecular nitric acid lines, the nitronium ion line, the strong hydrogen sulphate ion line at 1050 cm.$^{-1}$, the second hydrogen sulphate ion line at 590 cm.$^{-1}$, an unresolved low-frequency satellite to the nitric acid line 925 cm.$^{-1}$, which could be the third hydrogen sulphate frequency 895 cm.$^{-1}$, and the possible hydrogen sulphate line mentioned above. The spectrum of pure nitric acid contains molecular nitric acid lines, the nitronium ion line, and a line at 1050 cm.$^{-1}$, which will be shown in Part V to belong to the nitrate ion.

The spectra of all mixtures of intermediate composition contain the strong hydrogen sulphate ion frequency 1050 cm.$^{-1}$. It is interesting to observe what happens to the weaker hydrogen sulphate ion frequencies as the composition of the mixture changes progressively.

Consider first the frequency 590 cm.$^{-1}$. As the proportion of nitric acid in the mixed acids is increased from 0% to 90% the frequency at the intensity maximum of the relevant Raman line gradually shifts from 562 cm.$^{-1}$ to 585 cm.$^{-1}$. The former limit is the molecular sulphuric acid frequency, whilst the latter is essentially the hydrogen sulphate ion frequency. At no intermediate composition are the molecular sulphuric acid line and the hydrogen sulphate ion line resolved from each other: at all such compositions they build up an overlap intensity which is greater than the peak intensity of either component, with the result that the frequency of the observed intensity maximum shifts gradually as the composition of the mixture is progressively altered. That this is the behaviour which should be expected from the interpretation given is clear from recorded observations on the Raman spectra of mixtures of sulphuric acid and water, such as have been investigated by Bell and Jeppersen (*J. Chem. Physics*, 1935, **3**, 245) and by Woodward and Horner (*loc. cit.*). By increasing the proportion of water in such mixtures from 0% to 90% in stages of 5%, Bell and Jepperson were able to observe only a gradual shift, from 562 cm.$^{-1}$ to 592 cm.$^{-1}$, of the Raman frequency under consideration, without the least sign of resolution at any intermediate stage.

The third hydrogen sulphate ion frequency, 895 cm.$^{-1}$, lies so close to the molecular sulphuric acid frequency, 910 cm.$^{-1}$, that we must expect a similar gradual shift of the relevant Raman line, when the compositions of mixtures containing sulphuric acid are so changed that the content of hydrogen sulphate ion is progressively increased at the expense of the sulphuric acid molecules. Such an effect was, indeed, observed in the work already cited on mixtures of sulphuric acid with water. Thus, on increasing the content of water from 0% to 90%, Bell and Jepperson observed only a gradual fall, from 912 cm.$^{-1}$ to 895 cm.$^{-1}$, of the Raman frequency. Our result is more complex, *viz.*, that as the content of nitric acid in the mixed acids is increased from 0% to 30% the frequency of the relevant Raman line drops from 912 cm.$^{-1}$ to 904 cm.$^{-1}$; but that, on further increasing the proportion of nitric acid, the frequency rises again, its final value in 100% nitric acid being 925 cm.$^{-1}$. The evident interpretation is that the initial fall of frequency is caused by the partial replacement of sulphuric acid molecules by hydrogen sulphate ions, with partial emergence of the hydrogen sulphate ion line of frequency 895 cm.$^{-1}$ from eclipse by the sulphuric acid line at 910 cm.$^{-1}$; and that the subsequent rise in the observed frequency is caused by the incursion, in increasing proportion, of nitric acid molecules, and the consequent resubmergence of the hydrogen sulphate ion line in the strong and broad nitric acid line at 925 cm.$^{-1}$.

* Gillespie has shown (*J.*, 1950, 2493, 2516) that pure sulphuric acid contains both hydrogen sulphate and hydrogen disulphate ions, but in quantities too small for detection by present methods.

Reviewing this evidence, we conclude that all those spectral appearances are found which are to be expected on the basis of the theory that mixtures of nitric and sulphuric acid develop hydrogen sulphate ion in approximate accordance with the chemical equation already given.

(3.2) *Spectroscopic Detection of Perchlorate Ion in Mixtures of Nitric and Perchloric Acids.*—In our spectroscopic conditions, it is not possible with mixtures of nitric and perchloric acids, as it is with mixtures of nitric and sulphuric acids, to photograph Raman spectra over the whole range of compositions; because solid substances separate from the mixtures of nitric and perchloric acids, unless a large excess of one of these acids is present. We have given most attention to mixtures containing a large excess of nitric acid, for two reasons. One is that, in these mixtures, perchloric acid molecules are found to have been destroyed so completely that it is a relatively easy matter to prove the presence of perchlorate ions, and, indeed, to show that the whole of the added perchloric acid has been converted into perchlorate ions. The second reason is that, as reported in Section 2.2, we were concerned to establish the absence of an active frequency at 1050 cm.$^{-1}$; and, in this demonstration, the presence of any trace of molecular perchloric acid is an embarrassment, because the strongest line in the Raman spectrum of molecular perchloric acid lies at 1032 cm.$^{-1}$, quite close to the critical part of the spectrum.

A set of frequency measurements, which have been made on the Raman spectrum of a mixture of 10 mols. % of perchloric acid with 90 mols. % of nitric acid, is recorded in Table III. The frequencies are arranged in order to show such relation as they may have to the Raman frequencies of (i) anhydrous nitric acid, (ii) anhydrous perchloric acid, and (iii) the perchlorate ion as observed in aqueous sodium perchlorate. The data for perchloric acid and the perchlorate ion are due to Redlich, Holt, and Bigeleisen (*J. Amer. Chem. Soc.*, 1944, **66**, 13).

TABLE III.

Raman frequencies of a mixture of nitric and perchloric acids. Comparison with the Raman frequencies of anhydrous nitric acid, anhydrous perchloric acid, and aqueous sodium perchlorate.

(Frequency separations in cm.$^{-1}$ from Hg 4358 A.)

Anhydrous HNO_3.	$HClO_4$ (10 mol. %); HNO_3 (90 mol. %).	Aqueous $NaClO_4$.	Anhydrous $HClO_4$.
—	—	—	425 (w)
—	463 (mw) ———	464 (m)	—
—	—	—	572 (m)
—	—	—	585 (mw)
609 (ms) ———	616 (m)	—	—
—	—	631 (ms)	—
677 (ms) ———	678 (ms)	—	—
—	—	—	738 (m)
925 (s) ———	938 (s)	—	—
—	—	940 (vs)	—
—	—	—	1032 (s)
1049 (w)	—	—	—
—	—	1053—1167 (w, band)	—
—	—	—	1182—1312 (w, band)
1296 (vs) ———	1307 (vs)	—	—
1392 (w) - - - - - - - - - -	1397 (s)	—	—
1533 (w)	—	—	—
1670 (ms) ———	1679 (m)	—	—

It is evident from these figures that none of the molecular perchloric acid lines, not even the strongest at 1032 cm.$^{-1}$, appears in the spectrum of the mixture. It is also plain that all the molecular nitric acid lines, except the weakest at 1533 cm.$^{-1}$, are measured in the spectrum of the mixture. One weak line in the spectrum of anhydrous nitric acid, that near 1400 cm.$^{-1}$, is greatly intensified in the spectrum of the mixture: this is the nitronium ion line (cf. Section 2.3). Another weak line in the spectrum of anhydrous nitric acid, that near 1050 cm.$^{-1}$, is absent (cf. Fig. 1*a*) from the spectrum of the mixture: this is the nitrate ion line (cf. Part V). Having dealt with these frequencies, we shall now show that all those appearances in the spectrum of the acid mixture which still remain for consideration are to be attributed to the perchlorate ion.

This tetrahedral ion possesses four fundamental frequencies all active in the Raman effect. By far the strongest is the totally symmetrical frequency, 940 cm.$^{-1}$. It is not only strong, but also sharp. In the Raman spectrum of the mixture, this strong and sharp perchlorate ion line at 940 cm.$^{-1}$ overlaps the strong and broad nitric acid line at 925 cm.$^{-1}$. Although

molecular nitric acid is in large excess over perchlorate ion, the combined line derives its peak frequency, 938 cm.$^{-1}$, essentially from the perchlorate ion component, because of the sharpness of this frequency. Of course, the combined line derives its breadth essentially from the nitric acid component.

The next perchlorate ion frequency in order of strength is 631 cm.$^{-1}$, which belongs to one of the degenerate bending vibrations. This Raman line is rather broad, as also is the neighbouring nitric acid line at 609 cm.$^{-1}$. In the spectrum of the acid mixture, these two lines coalesce, giving, as might be expected, an overlap intensity having its maximum at a frequency, 616 cm.$^{-1}$, lying between the frequencies of the separate components.

The third frequency of the perchlorate ion, 464 cm.$^{-1}$, belongs to the other degenerate bending vibration. It is not very strong in the Raman effect, but it happens to lie in a region in which it can be observed without disturbance from nitric acid lines. Consistently we find this frequency in the spectrum of the acid mixture, in exactly the right position, and with the expected breadth and intensity.

The fourth fundamental frequency of the perchlorate ion belongs to the triply degenerate stretching vibration. It is represented in the Raman spectrum by the faint, diffuse band • at 1053—1167 cm.$^{-1}$. This band cannot be photographed except with the aid of long exposures. As was explained in Section 1.3, long exposures are inapplicable to all mixtures containing nitric acid in proportions greater than about 80%, because yellow material is developed, which absorbs the Raman radiation. Thus the weak band of the perchlorate ion spectrum is not observed in the spectrum of the mixture; but it is not an appearance which we can expect to observe. Summarising, we may say that, without exception, all those appearances are observed in the spectrum of the mixed acids which the presence of the perchlorate ion is expected to produce.

TABLE IV.

Raman frequencies of a mixture of nitric and selenic acids. Comparison with the Raman frequencies of anhydrous nitric acid, anhydrous selenic acid, and aqueous selenic acid.

(Frequency separations in cm.$^{-1}$ from Hg 4358 A.)

Anhydrous HNO_3.	H_2SeO_4 (12 mol. %); HNO_3 (88 mol. %).	H_2SeO_4 (92·5%); H_2O (7·5%).	Anhydrous H_2SeO_4.
—	296 (mw)	299 (ms)	294 (m)
—	350 (mw)	374 (ms)	361 (ms)
			388 (ms)
609 (ms)	618 (ms)	—	—
677 (ms)	678 (ms)	—	—
—	742 (ms)	747 (s)	756 (vs)
—	867 (ms)	862 (ms)	—
—	—	—	914 (s)
925 (s)	933 (s)	927 (mw)	—
—	—	951 (w)	—
—	—	—	996 (m)
1049 (w)	—	—	—
1296 (vs)	1306 (vs)	—	—
1392 (w)	1398·4 (s)	—	—
1533 (w)	1540 (w)	—	—
1670 (m)	1680 (m)	—	—

(3.3) *Spectroscopic Detection of Hydrogen Selenate Ion in Mixtures of Nitric and Selenic Acids.*—It is not conveniently possible in our conditions to record Raman spectra of mixtures of nitric and selenic acids over the total range of compositions, because selenic acid is a solid at ordinary temperatures. Again we have studied principally mixtures containing a large excess of nitric acid. A set of frequencies is given in Table IV, which have been measured in the Raman spectrum of a mixture of 12 mols. % of anhydrous selenic acid with 88 mols. % of anhydrous nitric acid. The set of frequencies is arranged in the Table in order to show such relation as they have to the known Raman frequencies of nitric acid and of selenic acid, as well as to the frequencies of the hydrogen selenate ion, as far as these are known from observations on the Raman spectra of aqueous selenic acid. The Raman frequencies which are quoted in the Table for anhydrous selenic acid and for an aqueous selenic acid containing 7·5% by weight of water are due to Venkateswaran (*Proc. Indian Acad. Sci.*, 1936, *A*, **3**, 3070).

• The reason why this fundamental vibration is represented by a band, and not by a line, is explained in Part IV (*J.*, 1930, paper no. 509).

The most obvious feature of the spectrum of the acid mixture is that it contains all the lines of molecular nitric acid. The nitronium ion frequency and the nitrate ion frequency, which appear weakly in the spectrum of molecular nitric acid, behave in the spectrum of the acid mixture, exactly as they do in that of the mixture with perchloric acid: the former frequency becomes greatly intensified, whilst the latter disappears. Apart from all these frequencies, the spectrum of the acid mixture contains four others, *viz.*, 296, 350, 742, and 867 cm.$^{-1}$, which are obviously connected with either the hydrogen selenate ion or the selenic acid molecule, and therefore require further discussion.

Similarly to sulphuric acid and the hydrogen sulphate ion, selenic acid and the hydrogen selenate ion possess a number of Raman frequencies which are nearly identical, each with each, whilst some Raman frequencies of the molecule, and some of its anion, are distinct, and therefore are of diagnostic value. Let us consider first these characteristic frequencies. The selenic acid molecule has two, *viz.*, those represented by the strong Raman line at 914 cm.$^{-1}$, and by the line of moderate intensity at 996 cm.$^{-1}$. Neither can be seen in the Raman spectrum of the mixed acids. The former might be difficult to observe in the presence of the nitric acid line at 925 cm.$^{-1}$, but the latter should be easily visible if molecular selenic acid were present. Therefore it is clear that molecular selenic acid is absent.

The hydrogen selenate ion has a highly characteristic frequency 862 cm.$^{-1}$. It is almost certainly a " breathing " frequency, corresponding to the frequency 1050 cm.$^{-1}$ of the hydrogen sulphate ion. It is well separated from any line of the selenic acid molecule, and from any line in the nitric acid spectrum. We find it well developed in the spectrum of the acid mixture. It is therefore certain that this mixture contains hydrogen selenate ion. Indeed, it is evident, taking account of the absence of the selenic acid frequencies, that practically the whole of the originally added selenic acid must have been converted into hydrogen selenate ion. The hydrogen selenate ion also has a characteristic, but rather weak, line at 927 cm.$^{-1}$, with a still weaker satellite at 951 cm.$^{-1}$; but these lines are of no diagnostic value in the present case, owing to the strong and broad nitric acid line at 925 cm.$^{-1}$, which obscures them.

The other three frequencies which we observe in the spectrum of the acid mixture, *viz.*, 296, 350, and 742 cm.$^{-1}$, are all frequencies which are approximately identical in the hydrogen selenate ion and the selenic acid molecule. As to the first two, this conclusion was drawn by Venkateswaran himself; but it is equally applicable to the third, as his records of observed intensities show. In the spectrum of the acid mixture, these three frequencies must come from the hydrogen selenate ion.

The four Raman frequencies, 296, 350, 742, and 867 cm.$^{-1}$, comprise all the known frequencies in the hydrogen selenate ion spectrum, apart from such as would be obscured by the Raman lines of nitric acid. Thus, not only does no feature of the spectrum of the acid mixture remain unexplained, but also all appearances which are to be expected from the presence of the hydrogen selenate ion are observed.

(4) *Reversibility of the Ionisation of Nitric Acid in Very Strong Acids.*

The effect of the spectral analyses described in Sections (2) and (3) has been to establish the formation of all the ions shown on the right-hand sides of the following equations, excepting the hydroxonium ion, which, as is well known, cannot be detected in Raman spectra:

$$HNO_3 + 2HClO_4 = NO_2^+ + H_3O^+ + 2ClO_4^-$$
$$HNO_3 + 2H_2SO_4 = NO_2^+ + H_3O^+ + 2HSO_4^-$$
$$HNO_3 + 2H_2SeO_4 = NO_2^+ + H_3O^+ + 2HSeO_4^-$$

It has been shown also that, in the presence of an excess of nitric acid, the whole of the second acid is destroyed; whilst, in the presence of excess of sulphuric acid, the whole of the nitric acid is destroyed.

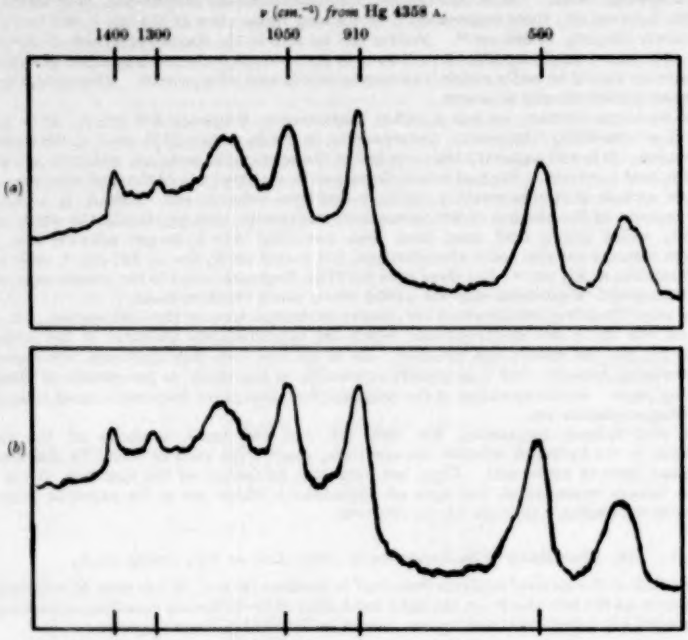
We describe in this Section an experiment which definitely establishes, in the example of the reaction between nitric and sulphuric acids, the reversibility of the closely analogous reactions written above. The method employed is essentially the same as that by which Chédin proved the dehydrating character of the action of sulphuric acid on nitric acid, by following the restoration of molecular nitric acid on adding water. In our experiment, a mixture of nitric and sulphuric acids was prepared, with the constituents in such proportions that almost all the molecular nitric acid was converted into nitronium ion. This solution was then divided into two parts, to one of which potassium hydrogen sulphate was added. Then the Raman spectra of the untreated and hydrogen-sulphate-treated mixtures were recorded under identical optical

conditions. A comparison of the spectra showed that the added potassium hydrogen sulphate had produced a partial regeneration of nitric acid molecules.

This experiment is illustrated by the microphotometric records shown in Fig. 3. Record (*a*) relates to a solution of 12·5% by weight of nitric acid in 87·5% of sulphuric acid. Record (*b*) relates to a part of the same solution which has been saturated with potassium hydrogen sulphate before the exposure.

FIG. 3.

Microphotometer records of parts of the Raman spectra, excited by Hg 4358 A. *filtered through nitrite, of* (a) *a solution,* 12·5% *by weight, of nitric acid in sulphuric acid, and* (b) *the same solution after being saturated with potassium hydrogen sulphate. (Most of the contour of the line at* 1400 cm.$^{-1}$ *is absent, because the extreme sharpness of this line causes the recording light ray of the microphotometer to travel over the recording paper too rapidly to leave a clearly visible trace.)*



Spectrum (*a*) contains all the stronger Raman lines of molecular sulphuric acid. It also contains, very strongly developed, the nitronium ion frequency, 1400 cm.$^{-1}$, and the strong and characteristic hydrogen sulphate ion frequency, 1050 cm.$^{-1}$. It shows the marked dissymmetry and broadening of the sulphuric acid line at 560 cm.$^{-1}$, and the similar but weaker appearance associated with the sulphuric acid line at 910 cm.$^{-1}$, effects which, as we saw in Section 3.1, arise from the presence of the hydrogen sulphate ion. It shows one further line, appearing with rather less than moderate intensity, *viz.*, the line at 1300 cm.$^{-1}$. This is the strongest line in the Raman spectrum of nitric acid, and, in record (*a*), it constitutes all that can be seen of the spectrum of molecular nitric acid.

Spectrum (*b*) contains all the stronger lines of molecular sulphuric acid, and the strongly developed nitronium ion line, as well as the characteristic hydrogen sulphate ion frequency, and those contour-deformations of sulphuric acid lines which are caused by the hydrogen sulphate ion. It is to be noted that all the spectral effects directly due to the hydrogen sulphate ion are stronger than before. Thus, the contour of the hydrogen sulphate ion line at 1050 cm.$^{-1}$ now stands up higher relatively to other lines; and the sulphuric acid lines at 560 cm.$^{-1}$ and 910 cm.$^{-1}$

are each appreciably thicker and more dissymmetric than before. The most interesting relative difference of intensity, however, relates to the remaining line in the spectrum, *viz.*, the molecular nitric acid line at 1300 cm.$^{-1}$. This is approximately twice as intense in record (*b*) as in record (*a*), clearly showing that molecular nitric acid has been regenerated by the added potassium hydrogen sulphate.

We thank Imperial Chemical Industries Limited, who have financially assisted the work described in this and the following papers.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, December 17th*, 1949.]

---

507. *Vibrational Spectra of Ionic Forms of Oxides and Oxy-acids of Nitrogen. Part II. Raman Spectra of Solutions in Sulphuric Oleum. The Polysulphuric Acids. Ionisation of Nitric Acid in Oleum.*

By D. J. MILLEN.

Chédin's observations on the Raman spectra of fuming sulphuric acid of various concentrations are analysed. The frequencies are separated into those belonging to H_2SO_4, $H_2S_2O_7$, $H_2S_3O_{10}$, $H_2S_4O_{13}$, or higher poly-acids, and SO_3. Spectral characteristics suitable for the detection of the different polysulphuric acids are pointed out.

New observations are recorded on the Raman spectra of solutions of sulphates in oleum of concentrations in the range over which disulphuric acid is the most important polysulphuric acid. These spectra are analysed. The frequencies, collectively assigned to disulphuric acid, are separated into those belonging to the molecular, and to each of the anionic, forms, $H_2S_2O_7$, $HS_2O_7^-$, $S_2O_7^{--}$. Their spectral identification is discussed.

Chédin's observations on the Raman spectra of solutions of nitric acid in oleum are supplemented by some new observations. All these results are now chemically interpreted on the basis of the above spectral analyses. The following conclusions are drawn. (1) In a dilute solution of nitric acid in dilute or moderately dilute oleum, the following reaction takes place nearly completely :

$$HNO_3 + 2H_2S_2O_7 = NO_2^+ + HS_2O_7^- + 2H_2SO_4$$

(2) On the addition of sufficient nitric acid to a dilute or moderately dilute oleum, the following reaction occurs nearly completely :

$$HNO_3 + H_2S_2O_7 = NO_2^+ + HSO_4^- + H_2SO_4$$

(3) In more concentrated oleum, and with correspondingly more concentrated nitric acid, the second reaction does not go nearly to completion, because its products tend to revert to those of the first reaction, in consequence of the following balanced process, which shifts towards the right with increasing concentration :

$$2NO_2^+ + 2HSO_4^- = NO_2^+ + HS_2O_7^- + HNO_3$$

All this is in good agreement with the cryoscopic and preparative chemical evidence.

THE Raman spectra of mixtures of nitric acid with fuming sulphuric acid have been extensively studied by Chédin. His results are now supplemented, and the interpretation revised. It will be necessary to refer first to the Raman spectra of the sulphuric oleums themselves, and then to the spectra given by sulphates dissolved in oleum of various strengths; only then shall we be in a position to discuss the spectra given by mixtures of nitric acid with fuming sulphuric acid.

(1) *Raman Spectra of Sulphuric Oleums.*

(1.1) *Dependence of the Spectrum on the Strength of the Oleum.*—The "strength" of an oleum will be designated as usual by the content of sulphur trioxide, supposing sulphur trioxide and sulphuric acid to be the sole components of oleum. An x% oleum is that which could be made by mixing $100 - x$ parts by weight of pure sulphuric acid with x parts of sulphur trioxide.

In an accompanying paper (*J.*, 1950, 2516) Gillespie offers cryoscopic evidence to the effect that fuming sulphuric acid contains, not only disulphuric acid, $H_2S_2O_7$, but also trisulphuric acid, $H_2S_3O_{10}$, and tetrasulphuric acid, $H_2S_4O_{13}$; it may contain still higher polysulphuric acids, as well as free sulphur trioxide. The work now to be described gives support to this view of the constitution of oleum.

The Raman spectra of oleums have been studied by Gopala Pai (*Phil. Mag.*, 1935, **20**, 616) and by Chédin (*Compt. rend.*, 1935, **201**, 724; *Ann. Chim.*, 1937, **8**, 243). Some of Chédin's

results are quoted in Table I. It will be convenient to note that a 45%, a 62%, and a 71% oleum have the compositions of di-, tri-, and tetra-sulphuric acid, respectively.

As sulphur trioxide is added progressively to pure sulphuric acid, the Raman lines of molecular sulphuric acid diminish in intensity and finally disappear, the strongest lines vanishing at compositions approximating to 45% oleum, as we should expect from the fact that the freezing-point curve passes through a maximum at this composition.

TABLE I.

Raman frequencies (cm.$^{-1}$) of sulphuric acid (after Chédin).

H_2SO_4.	10% Oleum.	23% Oleum.	36% Oleum.	51% Oleum.	65% Oleum.
—	—	—	—	246 (w)	245 (mw)
—	315 (mw)	305	300 (w)	297 (w)	295 (w)
		327 (m)	325 (m)	331 (m)	330 (m)
395 (ms)	388 (m)	390 (mw)	—	—	—
430 (ms)	427 (m)	427 (mw)	—	—	—
—	—	—	480 (w)	480 (mw)	484 (mw)
—	—	—	525 (w)	535 (mw)	536 (m)
560 (ms)	562 (m)	565 (m)	565 (w)	—	—
—	—	—	—	688 (w)	688 (m)
—	735 (w)	740 (m)	735 (m)	740 (ms)	737 (m)
917 (s)	915 (ms)	915 (m)	904 (mw)	—	—
972 (mw)	970 (mw)	975 (mw)	957 (mw)	960 (mw)	957 (m)
—	—	—	—	1075 (mw)	1075 (s)
1140	1140	1160	1160 (m)	—	—
—	—	1240	1250 (ms)	1250 (ms)	1252 (ms)
1370	1393	1420	1440 (mw)	1450 (m)	1450 (m)

(1.2) *Raman Frequencies of Disulphuric Acid.*—Before the spectrum of sulphuric acid has completely vanished, as the strength of the oleum is increased, a new spectrum makes its appearance. It consists of six frequencies, which can plausibly be assigned to disulphuric acid. Two of them, 325 and 735 cm.$^{-1}$, are prominent and characteristic : they can be used to diagnose the presence of disulphuric acid. Two more, 1240 and 1440 cm.$^{-1}$, are moderately strong, but appear to be the common possession of disulphuric acid, and at least one, possibly several, of the higher polysulphuric acids. A further one, 960 cm.$^{-1}$, is certainly possessed by sulphuric acid, and appears to be common to this acid, to disulphuric acid, and at least one, perhaps several, of the higher polysulphuric acids. The last frequency, 300 cm.$^{-1}$, appears as a satellite of the lowest of those already mentioned ; but it is weak, and sometimes remains unresolved in the spectrum. These assignments may here be summarised :

$H_2S_2O_7$ { 325, 735 cm.$^{-1}$ (strong, diagnostic) ; 300 cm.$^{-1}$ (weak)
1240, 1440 cm.$^{-1}$ (in common with higher poly-acids)
960 cm.$^{-1}$ (in common with H_2SO_4 and higher acids)

(1.3) *Raman Frequencies of Trisulphuric Acid.*—When the strength of the oleum is increased further, two additional lines appear. Their frequencies are 480 and 530 cm.$^{-1}$; and their intensities increase sharply, while those of the lines already assigned as characteristic of disulphuric acid either remain the same or begin to fall. Evidently these new lines mark the incursion of some new substance in the oleum ; and, as this is the first incursion of the kind since disulphuric acid made itself manifest in the spectrum, it is natural to identify the new material as trisulphuric acid.

The frequency 480 cm.$^{-1}$ appears to be characteristic of trisulphuric acid. The frequency 530 cm.$^{-1}$ seems to be equally diagnostic, provided that the oleum for which it is observed is not too strong. This qualification is necessary because very strong oleum contains free monomeric sulphur trioxide in sufficient amount to produce its own spectrum, and this contains a fairly prominent Raman line near 530 cm.$^{-1}$. Nevertheless the first appearance of the frequency 530 cm.$^{-1}$, when, starting with pure sulphuric acid, the strength of the oleum is gradually increased, cannot be ascribed to free sulphur trioxide, because at that stage of concentration the much stronger sulphur trioxide frequency, 1075 cm.$^{-1}$, is not yet showing.

A study of the intensities of the Raman lines of oleum, as functions of the strength of the oleum, shows that the source of the frequencies 480 and 530 cm.$^{-1}$ also has active frequencies coincident with, or quite close, to some of the active disulphuric acid frequencies ; these are 960, 1250, and 1450 cm.$^{-1}$. The following is a summary of the frequencies here assigned to trisulphuric acid :

$H_2S_3O_{10}$ { 480 cm.$^{-1}$ (strong, diagnostic)
530 cm.$^{-1}$ (strong, diagnostic except in strong oleum)
960, 1250, 1450 cm.$^{-1}$ (in common with other acids)

(1.4) *Raman Frequencies of Tetrasulphuric Acid, etc.*—When the strength of the oleum is increased still further, several new lines appear, notably those at 245, 688, and 1075 cm.$^{-1}$. These lines gain considerably in intensity with continued increase in the strength of the oleum; and so also does one of the previously assigned lines, *viz.*, that at 530 cm.$^{-1}$, although all the other lines which are considered to be characteristic of di- and tri-sulphuric acid become weaker or remain of about the same intensity. These new appearances and intensifications clearly mark the intrusion of a new substance, or, possibly, of several new substances in overlapping ranges of concentration. Three compounds, or types of compound, might be considered for assignment to the frequencies concerned, *viz.*, monomeric sulphur trioxide, the polymeric forms of sulphur trioxide, and polysulphuric acids higher than trisulphuric acid. We shall consider these in turn.

Sulphur trioxide, a planar trigonal molecule (Palmer, *J. Amer. Chem. Soc.*, 1938, **60**, 2360), has three fundamental frequencies allowed in the Raman spectrum (cf. Gerding and Lecomte, *Physica*, 1939, **6**, 737). The totally symmetrical frequency, 1075 cm.$^{-1}$, is much the strongest of the three. The next in order of intensity is the bending frequency, 530 cm.$^{-1}$. The third, the degenerate stretching frequency, 1330 cm.$^{-1}$, is weak in the Raman spectrum. In view of the intensity and relative sharpness with which 1075 cm.$^{-1}$ appears in the Raman spectrum of strong oleum, it is almost certainly correct to assign it, as Chédin has done, to sulphur trioxide; and, the presence of sulphur trioxide being admitted, it seems reasonable to attribute to the same substance the observed intensification of the frequency 530 cm.$^{-1}$.

The Raman spectrum of those polymeric forms of sulphur trioxide which are present in the liquid substance near the ordinary temperature has been studied by Bhagavantam (*Indian J. Physics*, 1930, **5**, 48), and by Gerding and his collaborators (*Z. physikal. Chem.*, 1937, **35**, *B*, 193, 216; *Rec. Trav. chim.*, 1937, **56**, 968). A large number of Raman frequencies have been observed, but it is difficult to establish any connexion between them and the oleum frequencies 245 and 688 cm.$^{-1}$, for which we wish now to account. For none of the frequencies of polymeric sulphur trioxide is close to 245 cm.$^{-1}$; and, although two of them are fairly close to 688 cm.$^{-1}$, they are represented by lines of only moderate intensity, and several stronger lines of the polymeric sulphur trioxide spectrum are absent from the oleum spectrum.

On these somewhat negative grounds, one inclines to the view that the frequencies 245 and 688 cm.$^{-1}$ belong to one or more of the polysulphuric acids higher than trisulphuric acid; and as they are amongst the first new frequencies to come into the spectrum, after those which are considered to characterise trisulphuric acid, when the strength of the oleum is increased, it seems natural to assign them to tetrasulphuric acid. A consideration of the intensities of other lines in the spectrum suggests that several of the frequencies of trisulphuric acid, notably 960 and 1250 cm.$^{-1}$, are also possessed by the source of the frequencies 245 and 688 cm.$^{-1}$. These further assignments may be summarised as follows:

$$H_2S_4O_{13}, \text{ etc.} \begin{cases} 245,\ 688 \text{ cm.}^{-1} \text{ (strong, diagnostic)} \\ 960,\ 1250 \text{ cm.}^{-1} \text{ (in common with other acids)} \end{cases}$$

It is concluded also that monomeric sulphur trioxide is present in quantity in oleums of strength above 50%; and that it is responsible for the frequency 1075 cm.$^{-1}$, and for part of the intensity of the frequency 530 cm.$^{-1}$. It appears that, in oleums of strengths up to 70%, the polymeric forms of sulphur trioxide are not present in sufficient amount to have a notable influence on the spectrum.

(2) *Raman Spectra of Solutions of Sulphates in Oleum.*

(2.1) *Preliminary Consideration of the Anions in Oleum.*—Before we can expect to be able to interpret the Raman spectra of solutions of nitric acid in oleum, it is necessary to know something of the spectral properties of the anions which are liable to be formed in oleum solutions. In dilute oleum, in which the principal molecular solute is disulphuric acid, the chief anions that can be produced by added substances, acting as bases in such solutions, are the hydrogen sulphate ion and the hydrogen disulphate ion. In the sulphuric acid solvent, disulphuric acid is an " acid " of medium strength, the hydrogen disulphate ion is the anion of a " neutral " salt, and the hydrogen sulphate ion is the strongest " base " that can exist in any considerable quantity in such a solution. These three entities bear the same sort of relation to one another as do acetic acid, the acetate ion, and the hydroxide ion, in solvent water. Thus molecular disulphuric acid and the hydrogen sulphate ion cannot coexist in any considerable concentration, but the hydrogen disulphate ion can coexist with either molecular disulphuric

acid or the hydrogen sulphate ion. All this is clear from the work of Gillespie on the freezing points of solutions of sulphates in oleums (*J.*, 1950, 2516).

There are some further matters to be taken into account, which also follow from Gillespie's results. The hydrogen disulphate *ion*, although called "neutral" as a first approximate description, is actually somewhat basic; for in the absence of free disulphuric acid it undergoes a limited, but appreciable, degree of solvolysis to the hydrogen sulphate ion. In addition, the hydrogen disulphate ion is a very weak acid, such as one might compare, for instance, with the hydrogen phosphate ion of an aqueous solution: in the presence of an excess of basic hydrogen sulphate ions, the hydrogen disulphate ion in a sulphuric acid solution is partly converted into the doubly charged disulphate ion.

In general, polysulphuric acids higher than disulphuric acid are present in oleum. However, the higher polysulphates are not expected to exist in sufficient amount in solutions of bases in weak oleums to have any notable effect on the spectra. On the other hand, a complicated situation could arise in solutions of bases in strong oleum in which the higher polysulphuric acids are present in important quantities.

(2.2) *Description of the Spectra.*—Table II contains a number of Raman frequencies, all measured as the frequency displacements of Stokes lines excited by Hg 4358 A. The figures in column 1 refer to sulphuric acid, which is the solvent throughout; they are given for comparison. So also are the figures in column 2, which relate to an oleum of the general type of those which were used for the preparation of solutions of sulphates. It is an oleum for which the spectrum of disulphuric acid is developed strongly, but the spectra of the higher polysulphuric acids, and the spectrum of sulphur trioxide, do not appear. The frequencies in the columns headed A—D refer to solutions of sulphates; and they are arranged in order of decreasing acidity and increasing basicity.

TABLE II.

Raman frequencies (cm.$^{-1}$) of solutions of sulphates in sulphuric oleum.

Pure H_2SO_4.	23% Oleum.	Sulphates in oleum.* A.	B.	C.	D.
—	316 (m)	317 (ms)	323 (m)	322 (m)	326 (vw)
395 (ms)	390 (mw)	386 (mw)	393 (mw)	396 (mw)	407 (m)
430 (ms)	427 (mw)	414 (mw)	423 (mw)	420 (mw)	vis. (m)
560 (ms)	565 (m)	570 (ms)	564 (ms)	561 (ms)	569 (ms)
—	740 (m)	735 (m)	734 (mw)	738 (mw)	vis. (vw)
917 (s)	915 (ms)	908 (s)	909 (s)	896 (s)	892 (s)
972 (mw)	975 (mw)	975 (w)	971 (w)	vis. (w)	—
—	—	—	—	1052 (m)	1042 (s)
—	—	1085 (w)	1081 (ms)	1085 (ms)	1092 (w)
1140	1160	1148	1171	1183	1180
—	1240	1227 (m)	1210 (mw)	} bands	bands
1370	1420	1391 (w)	1390 (mw)	}	

* The entry "vis." means that the Raman line was seen but not measured. The usual reason was that the intensity maximum was too smoothed-off to be accurately located.

Comparing the first two columns, one notices that the spectrum of the oleum exhibits all the stronger Raman frequencies which were shown in Section 1.2 to characterise disulphuric acid, notably the frequencies 325, 735, and 1240 cm.$^{-1}$.

The sulphate solution A is of an "acid" type. It is a moderately dilute solution of potassium hydrogen sulphate in excess of oleum; a quantitative statement of composition will be given later. All that need be noted now is that the composition is such as to leave disulphuric acid in excess, after the added hydrogen sulphate ion has been fully expended in decomposing disulphuric acid by the following proton-transfer process:

$$HSO_4^- + H_2S_2O_7 = H_2SO_4 + HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

This solution would be denoted by a point well to the right of the "neutral" line (the vertical line) in Gillespie's diagram (*J.*, 1950, 2521), and a little to the left of the sloping line which represents disulphuric acid as the only solute. On passing from the oleum itself to the sulphate solution A, the concentration of disulphuric acid will remain qualitatively similar. The only solute species which (apart from the spectrally non-significant potassium ion) exhibits a sharp relative increase of concentration on passing from the oleum to solution A is the hydrogen disulphate ion It follows that the spectrum of solution A can be understood if it is assumed that the newly appearing frequency 1083 $\pm$ 2 cm.$^{-1}$ (the frequency 1092 cm.$^{-1}$ will be shown to

have a different origin) belongs to the hydrogen disulphate ion (cf. also Part IV, *J.*, 1950, paper no. 509).

In Part I (*J.*, 1950, 2576) it was shown that the most characteristic frequency of the hydrogen sulphate ion is about 1050 cm.$^{-1}$, and that, indeed, this anion has no other Raman frequency that can be fully resolved from the frequencies of solvent sulphuric acid. In the spectrum of solution A we do not find the frequency 1050 cm.$^{-1}$, but we do find 1083 cm.$^{-1}$, a clear indication that, in the presence of a large excess of molecular disulphuric acid, the reaction of equation (1) proceeds to completion.

Solution B is " neutral," as this term applies to solutions in sulphuric acid. It is prepared by adding 1 mol. of ammonium sulphate to an oleum whose quantity and composition can be expressed by the statement that it contains 2 mols. of disulphuric acid. Since the reaction

$$SO_4^{--} + 2H_2S_2O_7 = H_2SO_4 + 2HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

may be assumed, the solution has the composition of a solution of ammonium hydrogen disulphate in sulphuric acid. It would be represented by a point on the neutral line of Gillespie's diagram.

In the Raman spectrum of this solution, the frequency 1083 cm.$^{-1}$ is found to be much intensified. This is intelligible, if, as is suggested, the frequency is characteristic of the hydrogen disulphate ion, which must be the principal solute here present, apart from the ammonium ion. The other significant result is that the frequencies 325, 735, and 1240 cm.$^{-1}$, although they appear more weakly than before, are not absent from the spectrum of this solution. There are two conceivable reasons for this. One is that the hydrogen disulphate ion is solvolysed, as may be represented by reading equation (1) from right to left, with the formation of a certain amount of molecular disulphuric acid, and also the hydrogen sulphate ion. However, it is difficult to believe that this is the main reason for the appearance of the three frequencies, because of the non-appearance of the frequency, 1050 cm.$^{-1}$, of the hydrogen sulphate ion. The alternative hypothesis is that the three frequencies of disulphuric acid are not the exclusive possession of the molecular form of the acid, but are common to the acid and its anion; for we must expect that molecular disulphuric acid and the hydrogen disulphate ion will have a number of nearly coincident frequencies, just as have sulphuric acid and the hydrogen sulphate ion (cf. Part I). A conclusion concerning this matter will be reached in Section 2.3. In further explanation of the observations, it should be mentioned that the highest of the three disulphuric acid frequencies is not satisfactorily measured, because of overlapping by the ammonium ion bands. The ammonium ion has, in theory, a doubly degenerate, and a triply degenerate, bending vibration; but in solution, the degeneracies are split, and the separated frequencies are broadened by hydrogen bonding until they merge into a continuous band, which extends over most of the spectral region 1200—1500 cm.$^{-1}$. Other frequencies in this neighbourhood may therefore be rendered difficult or impossible to measure.

Solution C is " basic." It is prepared by using twice the preceding proportion of ammonium sulphate. Since the reaction

$$SO_4^{--} + H_2S_2O_7 = HSO_4^- + HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

may be assumed, the solution may be described as containing an equimolecular mixture of the neutral solute, ammonium hydrogen disulphate, with the basic solute, ammonium hydrogen sulphate. The composition would be represented by a point on the left of the neutral line on Gillespie's diagram (*J.*, 1950, 2521), and close to a line (not drawn) which would pass through the freezing-point maxima in this region. Indeed, the composition is so chosen that it corresponds approximately to the end-point of the water-titration of oleum solutions (Gillespie, *loc. cit.*), and to the freezing-point maximum which is obtained by adding water to a solution of sulphates in oleum.

In the spectrum of this solution, we find side by side the diagnostic frequencies of the hydrogen sulphate and hydrogen disulphate ions, 1050 cm.$^{-1}$ and 1083 cm.$^{-1}$, the latter in rather greater spectral strength than the former. We also observe, though with a further slight diminution of intensity as compared with solution B, the two disulphuric acid frequencies 325 and 735 cm.$^{-1}$. The third of the disulphuric acid frequencies discussed above is obscured by the ammonium ion bands in this spectrum.

Solution D may be classified as strongly " basic." It would be represented by a point well down the descending branch of a freezing-point curve such as those which appear on the left of Gillespie's diagram. Four times the preceding proportion of ammonium sulphate was employed for the preparation of this solution. Assuming the reaction

$$4SO_4^{--} + H_2S_2O_7 + 3H_2SO_4 = 7HSO_4^- + HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad (4)$$

one could describe the solute as consisting of a mixture of 7 mols. of ammonium hydrogen sulphate with 1 mol. of ammonium hydrogen disulphate.

In the spectrum of solution D, the characteristic frequency of the hydrogen sulphate ion is strongly developed. The spectrum also contains a somewhat weak frequency 1092 cm.$^{-1}$. This value occurs so regularly when an excess of hydrogen sulphate ions is present, that one naturally connects it with the expected balanced reaction

$$HSO_4^- + HS_2O_7^- = H_2SO_4 + S_2O_7^{--} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

and assigns the frequency to the doubly charged disulphate ion (cf. also Part IV, *J.*, 1950, **2516**).

Microphotometer records of parts of the Raman spectra of the four sulphate solutions are reproduced in Fig. 1.

(2.3) *Frequencies of the Molecular and Anionic Forms of Disulphuric Acid.*—It is helpful to make some approximate calculations of the concentrations of the various entities which are present in the solutions whose Raman frequencies are recorded in Table II. The solution A was prepared from 8 parts by weight of potassium hydrogen sulphate and 100 parts of 30% oleum. Solutions B, C, and D were prepared from 33%, 25%, and 10% oleum, respectively, together with ammonium sulphate in the proportions stated already.

In these calculations, two equilibrium constants, due to Gillespie, are utilised, *viz.*, the first acidity constant of disulphuric acid, and the solvolysis constant for the hydrogen disulphate ion (cf. *J.*, 1950, **2516**). We are now concerned with solutions which are considerably more concentrated than those for which the equilibrium constants were determined, but it may be hoped that one can arrive at the correct orders of magnitude of the quantities in which we are interested by the use of these constants. Because the mol.-fraction of total solute is not now small in comparison with that of the solvent, it is convenient to re-express the equilibrium constants in forms which show the solvent concentration explicitly:

$$[H_2SO_4^+][HS_2O_7^-]/[H_4S_2O_7][H_2SO_4] = 0{\cdot}0020$$
$$[H_2S_2O_7][HSO_4^-]/[HS_2O_7^-][H_2SO_4] = 0{\cdot}00080$$

These constants are independent of the units of concentration, provided that they are molecular units.

Table III contains the calculated compositions of the different solutions. They are expressed as the number of molecules or ions of each species which are present in as much of a solution as would contain 100 atoms of sulphur—this being an amount which cannot be changed, as the total number of molecules and ions can be changed, by a shifting of some of the equilibria. For lack of knowledge of the second acidity constant of disulphuric acid, we cannot calculate the concentrations of normal disulphate ions, or take account of the other consequences of the balanced reaction (5). It is probable that a small proportion of what are calculated as hydrogen disulphate ions in solution C, actually exist as normal disulphate ions; and that a large proportion of what are entered as hydrogen disulphate ions in solution D really consist of normal disulphate ions.

TABLE III.

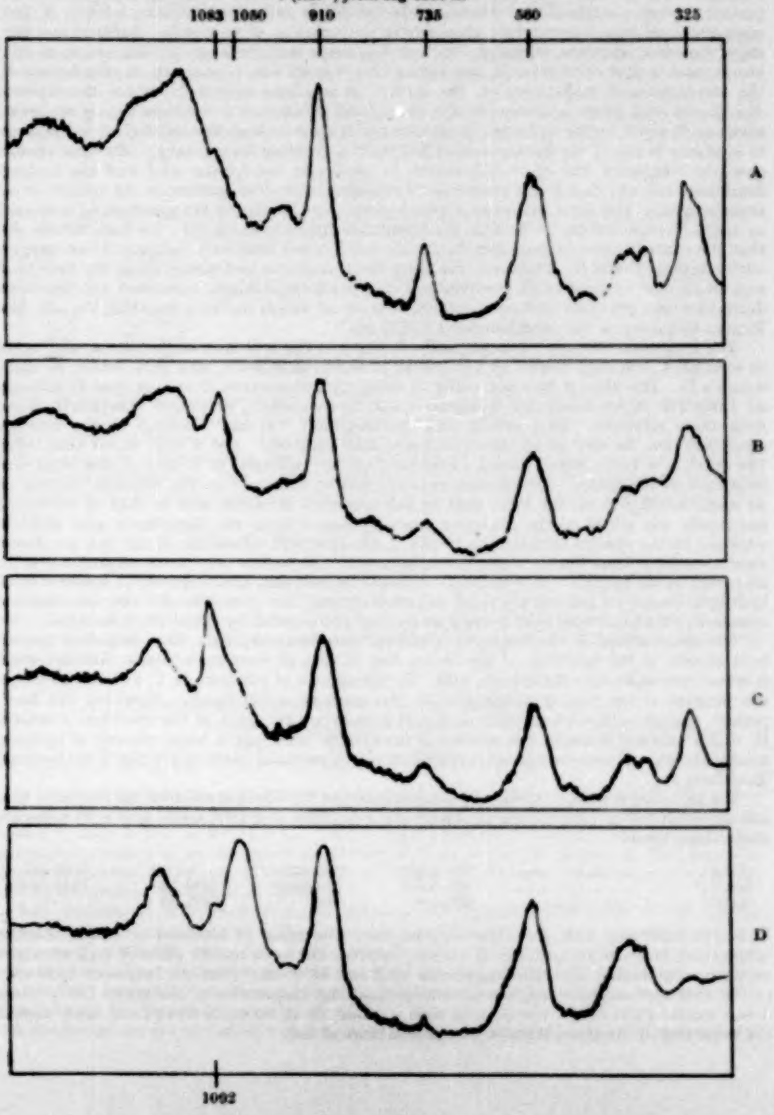
Calculated molecular compositions of the solutions of Table II.

	100% H_2SO_4.	23% Oleum.	Sulphate solutions. A.	B.	C.	D.
$H_2SO_4^+$	0·1	1·6	0·3	0·0	0·0	0·0
H_2SO_4	99·7	45·0	32·8	35·4	32·5	27·1
HSO_4^-	0·1	0·0	0·0	0·9	22·5	56·8
$H_4S_2O_7$	0·0	25·1	28·2	0·9	0·0	0·0
$HS_2O_7^-$	0·1	1·6	5·2	30·5	22·5	8·1

Let us consider, in the light of these figures, the variations of intensity, from one solution to another, of the different Raman lines representing the various solutes. We commence with the lines in the frequency region 1050—1090 cm.$^{-1}$, which are essentially characteristic of the anions. Taking account of the variations, from one solution to another, of the calculated concentration of the hydrogen disulphate ion, as given in Table III, it is intelligible that the frequency 1083 cm.$^{-1}$, which is assigned to, and considered to be diagnostic for, this ion, should not appear in the spectrum of sulphuric acid, or of the oleum, and should appear weakly in the spectrum of solution A, strongly in the spectra of solutions B and C, and again weakly in the spectrum of solution D. In the last-mentioned spectrum, the line occurs at the displaced frequency 1092 cm.$^{-1}$, and this, as has been noted already, may mean that its source in this spectrum is the normal disulphate ion. Again, a glance at the calculated concentrations of the

FIG. 1.

Microphotometer records of parts of the Raman spectra (Stokes lines excited by nitrite-filtered Hg 4358 A.*) of solutions of sulphates in oleum. As to the compositions of solutions* A, B, C, *and* D, *see the text. The frequencies 580 and 910 cm.$^{-1}$ belong to the solvent sulphuric acid, whilst 1030 cm.$^{-1}$ is assigned to the hydrogen sulphate ion, 1083 cm.$^{-1}$ to the hydrogen disulphate ion, and 1092 cm.$^{-1}$ to the normal disulphate ion; and 735 and 325 cm.$^{-1}$ are considered as common to the disulphuric acid molecule and the hydrogen disulphate ion, but with differences of intensity (see text).*



hydrogen sulphate ion, as given in Table III, renders it intelligible that the characteristic frequency 1050 cm.$^{-1}$, of this ion, should not be visible in the spectra of sulphuric acid, the oleum, and the sulphate solutions A and B, but should be prominent in the spectrum of solution C, and very strong in that of solution D.

New conclusions can be derived by applying this method of examination to the three frequencies 325, 735, and 1240 cm.$^{-1}$, which in Section 1.2 were assigned to disulphuric acid. Consider first the frequency 325 cm.$^{-1}$. Table III shows that molecular disulphuric acid is present in very considerable concentration in the oleum and in the sulphate solution A, but is completely, or almost completely, absent from the solutions B, C, and D. Table II and Fig. 1 show, however, that the frequency 325 cm.$^{-1}$ appears fairly strongly in the spectrum of the oleum, and in that of solution A, and suffers only a small loss of intensity, in comparison with the sulphuric acid frequencies, in the spectra of solutions B and C. Since the molecular disulphuric acid which is present in the oleum and in solution A becomes largely replaced in solutions B and C by the hydrogen disulphate ion, it must be from this anion that, in the spectra of solutions B and C, the Raman line at 325 cm.$^{-1}$ is deriving its intensity. We must conclude that the frequency 325 cm.$^{-1}$ is common to molecular disulphuric acid and the hydrogen disulphate ion, and that it has intensities of the same order of magnitude in the spectra of both these sources. The same frequency appears much more weakly in the spectrum of solution D, as might be expected on the basis of the calculated figures in Table III: for these figures show that the concentration of hydrogen disulphate ion is much reduced in solution D, as compared with solutions B and C. However, the same result could be understood along the lines of the suggestion that, in solution D, the hydrogen disulphate ion is largely converted into the normal disulphate ion, provided that one assumes, as is by no means unlikely, that this ion also has a Raman frequency in the neighbourhood of 325 cm.$^{-1}$.

The frequency 735 cm.$^{-1}$ appears fairly strongly in the spectrum of the oleum, and in that of solution A, but only weakly in the spectra of solutions B and C, and very weakly in that of solution D. However, it does not vanish in the spectra of solutions B or C, or even D, although, as Table III shows, molecular disulphuric acid is completely, or almost completely, absent from these solutions. This proves that the frequency 735 cm.$^{-1}$ belongs to the hydrogen disulphate ion, as well as to the disulphuric acid molecule; and it also shows that, whilst 735 cm.$^{-1}$ is a fairly strong Raman frequency of the molecule, it is only a somewhat weak frequency of the anion. The intensities of the line at 735 cm.$^{-1}$ in the different spectra can be made intelligible on the basis that in the spectrum of oleum, and in that of solution A, practically the whole of the observed intensity comes from the disulphuric acid molecule, whereas, in the spectra of solutions B and C, the observed intensities of the line are derived almost entirely from the hydrogen disulphate ion. As to the very weak appearance of the frequency in the spectrum of solution D, it might be held that this frequency is common to the hydrogen disulphate ion and the normal disulphate ion; but it is difficult to be sure that such a weak line does not arise from a small amount of unconverted hydrogen disulphate ion.

The observations on the frequency 1240 cm.$^{-1}$ are less complete. This frequency appears, as it should, in the spectrum of the oleum, and in that of solution A, where, without doubt, it arises from molecular disulphuric acid. In the spectra of solutions B, C, and D, the line, or the position of the line, is overlapped by the ammonium ion bands. However, the line is present, though with the somewhat displaced frequency 1210 cm.$^{-1}$, in the spectrum of solution B, which contains scarcely any molecular disulphuric acid, but a large amount of hydrogen disulphate ion. It therefore seems certain that this appearance of the line is due to the hydrogen disulphate ion.

The following is a list of frequency assignments (cm.$^{-1}$), which summarise the results of these considerations concerning the Raman-spectral characteristics of disulphuric acid in its molecular and anionic forms:

$H_2S_2O_7$	325 (ms)	735 (ms)	—	1240 (m)
$HS_2O_7^-$	325 (ms)	735 (mw)	1083 (s)	1210 (mw)
$S_2O_7^{--}$	325 (m)	735?	1092 (s)	?

It is not surprising that the three entities have a number of identical or nearly identical frequencies, because the mechanical coupling between the more remote parts of such structures must be very weak. Thus the frequencies 1083 and 1092 cm.$^{-1}$ (like the frequency 1050 cm.$^{-1}$ of the hydrogen sulphate ion) are obviously breathing frequencies of the group OSO_3^-; and it can matter little to the vibration of such a group, in an anion of disulphuric acid, whether the other end of the anion contains one proton more or less.

With regard to the problem of the spectroscopic detection of the forms of disulphuric acid, the anions can evidently be recognised by means of their characteristic frequencies 1083 and 1092 cm.$^{-1}$. When these are absent, the neutral molecule can be detected by means of the frequencies 325 and 735 cm.$^{-1}$. When the frequency 1092 cm.$^{-1}$ is present, the molecule may be assumed absent. When the frequency 1083 cm.$^{-1}$ is present, then the presence of the molecule has to be judged from the relative intensities of the frequencies 325 and 735 cm.$^{-1}$.

(3) *Raman Spectra of Solutions of Nitric Acid in Oleum.*

(3.1) *Identification of the Nitronium and Hydrogen Disulphate Ions.*—In Table IV the Raman frequencies are given which have been measured in the spectrum of a solution of 5 parts by weight of anhydrous nitric acid in 100 parts of 20% oleum (solution N). The lines measured were Stokes lines excited by nitrite-filtered Hg 4358 A. In the Table, the frequencies of these lines are compared with those of a solution of potassium hydrogen sulphate in oleum (solution A). An assignment of all these frequencies to their sources is given in the Table. The assignment is based to a considerable extent on the conclusions of Section 2.3.

TABLE IV.

Raman frequencies (cm.$^{-1}$) of a solution of nitric acid, and of a solution of potassium hydrogen sulphate, in oleum; and an assignment.

HNO_3 (Soln. N).	$KHSO_4$ (Soln. A).	Assignment.	HNO_3 (Soln. N).	$KHSO_4$ (Soln. A).	Assignment.
321 (mw)	317 (ms)	$H_2S_2O_7$ and $HS_2O_7^-$	983 (w)	975 (w)	H_2SO_4
387 (mw)	386 (mw)	H_2SO_4	1083 (w)	1085 (w)	$HS_2O_7^-$
419 (mw)	414 (mw)	,,	1158	1148	H_2SO_4
567 (ms)	570 (ms)	,,	1230 (mw)	1227 (m)	$H_2S_2O_7$ and $HS_2O_7^-$
735 (w)	735 (m)	$H_2S_2O_7$ (mainly)	Present	1391 (w)	H_2SO_4
914 (s)	908 (s)	H_2SO_4	1402 (m)	—	NO_2^+

It is notable that, in the spectrum of solution N, even the strongest lines of nitric acid do not appear. On the other hand, the presence of the sharp line at 1400 cm.$^{-1}$ shows that the solution contains nitronium ion. As to anions, neither the nitric acid solution nor the potassium hydrogen sulphate solution gives the Raman frequency 1050 cm.$^{-1}$, which is characteristic of the hydrogen sulphate ion; but both give the frequency 1083 cm.$^{-1}$, by which the hydrogen disulphate ion can be recognised. The reaction undergone by nitric acid is therefore essentially as follows:

$$HNO_3 + 2H_2S_2O_7 = NO_2^+ + HS_2O_7^- + 2H_2SO_4 \quad . \quad . \quad . \quad . \quad . \quad (6)$$

These conclusions may be confirmed by comparing the spectra with the calculated compositions of the solutions. Such compositions are given in Table V. They are calculated in the same way, and are expressed in the same form, as the compositions in Table III. It is assumed that nitric acid is quantitatively decomposed according to equation (6), and that then sulphuric and disulphuric acids come into equilibrium with each other, and with their ions, in the ways already described.

TABLE V.

Calculated molecular compositions of the solutions of Table IV.

	NO_2^+.	$H_2SO_4^+$.	H_2SO_4.	HSO_4^-.	$H_2S_2O_7$.	$HS_2O_7^-$.
Soln. N	7·9	0·2	66·7	0·0	8·4	7·6
Soln. A	0·0	0·3	32·8	0·0	28·2	5·2

As can be seen from the microphotometer records of the spectra reproduced in Fig. 2, the hydrogen disulphate ion frequency, 1083 cm.$^{-1}$, is appreciably stronger in the spectrum of solution N than in that of solution A. On the other hand, the frequencies 325 and 735 cm.$^{-1}$ are markedly weaker in the spectrum of solution N than in that of solution A, the difference being more marked in the case of the frequency 735 cm.$^{-1}$. All these differences can be understood on the basis of the figures in Table V.

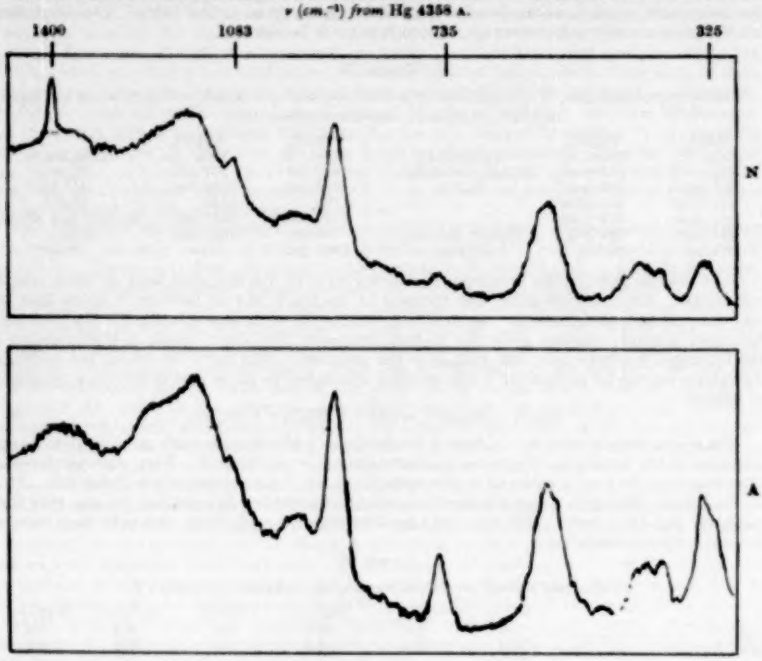
(3.2) *Stability of Nitronium Hydrogen Sulphate.*—A comprehensive study of the Raman spectra of mixtures of nitric acid with oleum of various strengths has been reported by Chédin (*Compt. rend.*, 1936, **202**, 220; *Ann. Chim.*, 1937, **8**, 243). It has not previously been possible to give a satisfactory interpretation of these spectra for lack of sufficient knowledge about the characteristic frequencies of the ions in such solutions. An interpretation is now offered, which is based on the conclusions of Section 2.3.

A condensed survey of Chédin's results (already partly interpreted as an aid to summaris-

ation) is given in Table VI. The data relate to various mixtures of anhydrous nitric acid with oleum of each of three different strengths. The "experimental" proportions of nitric acid, given in column 2, are the proportions which refer to the tabulated spectral particulars. The significance of the "calculated critical" proportions, in column 1, will be explained later. The observed frequencies are assigned either collectively, as in the case of the sulphuric acid frequencies, or individually, as with most of the ionic frequencies. Thus the Table shows which species are present at the different concentrations of added nitric acid, and the direction in

FIG. 2.

Microphotometer records of parts of the Raman spectra (Stokes lines excited by nitrite-filtered Hg 4358 A.*) of solutions of nitric acid* (N) *and potassium hydrogen sulphate* (A) *in oleum. As to compositions, see text. The frequency* 1400 $cm.^{-1}$ *belongs to the nitronium ion, whilst* 1083 $cm.^{-1}$ *arises from the hydrogen disulphate ion. Molecular disulphuric acid is the main source of the frequency* 735 $cm.^{-1}$, *whilst both disulphuric acid and the hydrogen disulphate ion contribute to the intensity of the line at* 325 $cm.^{-1}$.



which the concentration of each species changes as the proportion of added nitric acid is varied. In the spectra of mixtures with larger proportions of added nitric acid than those indicated in the Table, the stronger Raman lines of molecular nitric acid appear.

The proportions of nitric acid which are marked with an asterisk in column 1 of Table VI are those proportions which are calculated to be stoicheiometrically necessary for a complete decomposition of all solutes in the sulphuric acid solvent according to the equation

$$HNO_3 + 2SO_3 = NO_2^+ + HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

In this equation, oleum is taken as a system (in the thermodynamic sense) of the two components, sulphur trioxide and sulphuric acid, its detailed chemical constitution being irrelevant. With reagents in the calculated proportions, a complete reaction according to equation (7) should produce a solution of nothing but nitronium hydrogen disulphate in sulphuric acid. The spectrum of such a solution should show the presence of the nitronium ion, of the hydrogen

disulphate ion, and of the sulphuric acid molecule; and it should indicate the absence of the hydrogen sulphate ion, of the disulphuric acid molecule, and of the nitric acid molecule. It seems from Chédin's data that, the correct quantities of the reagents being supplied, this situation would very approximately be realised with mixtures made from oleum of all the strengths he investigated. It must be concluded that, in very concentrated, as well as in more dilute, solution in sulphuric acid, the group of reactions summarised in equation (7) tends to proceed nearly to completion.

TABLE VI.

Survey and interpretation of Chédin's Raman frequencies (cm.$^{-1}$) for mixtures of nitric acid with fuming sulphuric acid.

Wt. % HNO_3. Calc. / Exptl. crit.		NO_2^+ (~1400).	$HS_2O_7^-$ and $S_2O_7^{--}$ (~1090).	HSO_4^- (~1050).	$H_2S_2O_7$ and $HS_2O_7^-$ (~325).	$H_2S_2O_7$ mainly (~735).	H_2SO_4 lines.
Mixtures of HNO_3 *with 60% oleum:*							
19 *	10	1400	~1080	absent	330	735	absent
	20	,,	1080	,,	,,	v. weak	appear
33 †	30	,,	1094	1044	,,	absent	,,
	40 ‡	,,	1094	,,	,,	,,	,,
	—	strengthening	weakening	strengthening	weakening	,,	strengthening
Mixtures of HNO_3 *with 45% oleum:*							
15 *	10	1400	1086	absent	325	735	appear
26 †	20	,,	1091	,,	,,	absent	,,
	30	,,	absent	1040	,,	,,	,,
	—	strengthening	,,	strengthening	weakening	,,	strengthening
Mixtures of HNO_3 *with 35% oleum:*							
12 *	10	1401	1084	absent	323	737	appear
21 †	20	,,	absent	1040	absent	absent	,,
	30 ‡	,,	,,	,,	,,	,,	,,
	—	strengthening	,,	strengthening	,,	,,	strengthening

* Theoretical quantity for the production of $(NO_2^+)(HS_2O_7^-)$ as the only solute.
† ,, ,, ,, ,, $(NO_2^+)(HSO_4^-)$,, ,,
‡ Molecular HNO_3 lines were present in the spectra of these mixtures.

The proportions of nitric acid which are marked with a dagger on the left of Table VI are the proportions which would stoicheiometrically permit a complete decomposition of all solutes in the sulphuric acid solvent according to the equation

$$HNO_3 + SO_3 = NO_2^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

Here again, oleum is taken as a system of the components, sulphur trioxide and sulphuric acid, the manner of their combination being irrelevant. With reagents in the correct proportions, a complete reaction of this kind should produce a solution of nothing but nitronium hydrogen sulphate in sulphuric acid. Its spectrum should reveal the presence of the nitronium ion, of the hydrogen sulphate ion, and of the sulphuric acid molecule; and it should indicate the absence of the hydrogen disulphate or disulphate ion, of the disulphuric acid molecule, and of the nitric acid molecule. This would seem to be approximately the situation in a mixture involving the most dilute of Chédin's oleums. It might not be quite true, but it could not be very far from a correct description, in the intermediate case. But it would definitely not be true for a mixture made from the most concentrated of the oleums. In this case, as Chédin's results show, anions of disulphuric acid are present in quantity, side by side with the hydrogen sulphate ion, and even with the nitric acid molecule after more than enough nitric acid has been supplied to convert all forms of disulphuric acid into the hydrogen sulphate ion. (Incidentally, it is consistent with the results and discussion given in Sections 2.2 and 2.3 that, when an anion of disulphuric acid coexists with the hydrogen sulphate ion in these solutions, the former exhibits the higher frequency, 1092 cm.$^{-1}$, which is assumed to be indicative of the normal disulphate ion.) The general conclusion is that, in dilute solution in sulphuric acid, the group of reactions summarised in equation (8) tends to proceed nearly to completion; but that, in concentrated solution, no such nearly complete conversion takes place, the products of reaction (8) tending to revert to those of reaction (7) in the following balanced reaction:

$$2NO_2^+ + 2HSO_4^- = NO_2^+ + HS_2O_7^- + HNO_3 \quad . \quad . \quad . \quad . \quad . \quad (9)$$

These conclusions fall well into line with contemporaneously reported evidence of other

kinds. The cryoscopic data of Gillespie, Graham, Hughes, Ingold, and Peeling (*J.*, 1950, 2504) show that nitronium hydrogen sulphate is perfectly stable in dilute solution in sulphuric acid; and those of Gillespie and Graham (*J.*, 1950, 2532) prove the same for nitronium hydrogen disulphate in dilute solution. But there is a very distinct difference in the stability of the two salts in concentrated forms. As is shown by Goddard, Hughes, and Ingold (*J.*, 1950, 2559), nitronium hydrogen sulphate cannot be isolated in a pure condition, because, in the concentrated state, it loses nitric acid, yielding the easily isolated, much more stable salt, nitronium hydrogen disulphate. The last-named authors explained these observations on the basis of equation (9), describing the reaction as a dehydration of the anion of nitronium hydrogen sulphate by its own cation, or, more generally, as the extraction from the feebly nucleophilic anion of a more strongly nucleophilic portion (OH^-) by the very strongly electrophilic nitronium ion. Thermodynamically, it is axiomatic that a balanced reaction of the form represented in equation (9) must move towards the right as concentration is increased.

The author is indebted to Professor C. K. Ingold for invaluable help and advice.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, December 17th*, 1949.

---

508. *Vibrational Spectra of Ionic Forms of Oxides and Oxy-acids of Nitrogen. Part III. Raman Spectral Evidence of the Ionisation of Dinitrogen Trioxide, Dinitrogen Tetroxide, and Dinitrogen Pentoxide by Sulphuric Acid.*

By D. J. MILLEN.

Raman spectra of solutions of dinitrogen trioxide in sulphuric acid indicate that the following reaction takes place completely, slight incompleteness of the ionisation of water being neglected:

$$N_2O_3 + 3H_2SO_4 = 2NO^+ + 3HSO_4^- + H_3O^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

A quantity of added water that would be enough completely to destroy nitronium ion by converting it (cf. Part I, Section 4) into molecular nitric acid in reaction (3), is insufficient to convert a detectable amount of nitrosonium ion at identical concentrations in the analogous reaction (2):

$$NO^+ + 2HSO_4^- + H_3O^+ = HNO_2 + 2H_2SO_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$NO_2^+ + 2HSO_4^- + H_3O^+ = HNO_3 + 2H_2SO_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Thus, in thermodynamic comparison, the nitrosonium ion has a much smaller electrophilic reactivity towards water than has the nitronium ion.

Raman spectra of solutions of dinitrogen tetroxide in sulphuric acid show that, in dilute solution, the following reaction is quantitative except for the incompleteness of water ionisation:

$$N_2O_4 + 3H_2SO_4 = NO^+ + NO_2^+ + 3HSO_4^- + H_3O^+ \quad . \quad . \quad . \quad . \quad (4)$$

In more concentrated solution, the build-up of nitronium ion, and of the ions of water, by reaction (4) can be sufficient to allow the nitronium ion to show its thermodynamic instability by reacting with the water ions to form an appreciable amount of molecular nitric acid in the balanced process (3). Nothing analogous happens to the simultaneously formed nitrosonium ions, within the range of concentrations studied.

Raman spectra of solutions of dinitrogen pentoxide in sulphuric acid prove that, in dilute solution, the following reaction takes place quantitatively, apart from water ionisation:

$$N_2O_5 + 3H_2SO_4 = 2NO_2^+ + 3HSO_4^- + H_3O^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

In more concentrated solutions of dinitrogen pentoxide in sulphuric acid, the build-up of nitronium ions, and of the ions of water, by reaction (5) can again lead to appreciable production of molecular nitric acid by the balanced process (3). Thus the two reactions together constitute a hydration–dehydration disproportionation of dinitrogen pentoxide.

(1) *Ionisation of Dinitrogen Trioxide in Sulphuric Acid.*

(1.1) ***Raman-spectroscopic Properties of Nitrosonium Salts.***—A brief consideration of this subject is a necessary preliminary to the investigation of some of the Raman spectra described below.

Nitrosonium hydrogen sulphate has long been known as "chamber crystals" or "nitrosyl-sulphuric acid," and several non-ionic structures have been proposed for it. Hantzsch and Berger (*Z. anorg. Chem.*, 1930, **190**, 321) first showed that it behaved as a binary electrolyte in

sulphuric acid. They also brought forward evidence, based on its reactivity, that the ions are nitrosonium and hydrogen sulphate ions. They suggested that the solid compound had the ionic structure $(NO^+)(HSO_4^-)$, and proposed similar structures for other nitrosonium salts, such as the perchlorate and fluoroborate.

The Raman spectra of solid nitrosonium hydrogen sulphate, and of its solutions in sulphuric acid (Angus and Leckie, *Proc. Roy. Soc.*, 1935, **149**, 327), are all characterised by a line at approximately 2320 cm.$^{-1}$. The interpretation of these spectra is not entirely unambiguous, because of the presence of a number of other lines, whose origin is not clear. The interpretation of the Raman spectrum of nitrosonium perchlorate (Angus and Leckie, *Proc. Roy. Soc.*, 1935, *A*, **150**, 615) is, however, unequivocal. The frequencies of the solid, and of its solutions in aqueous perchloric acid of two concentrations, together with the well-established frequencies of the perchlorate ion (Redlich, Holt, and Bigeleisen, *J. Amer. Chem. Soc.*, 1944, **66**, 13), are quoted in Table I.

TABLE I.

Raman frequencies (in cm.$^{-1}$) of nitrosonium perchlorate (after Angus and Leckie).

Solid.	Solution in 62 wt. % $HClO_4$.	Solution in 48 wt. % $HClO_4$.	Perchlorate ion.
463 (m)	469 (ms)	450 (w)	464 (m)
703 (m)	633 (ms)	623 (m)	631 (ms)
929 (ms)	932 (ms)	930 (vs)	940 (vs)
1117 (vw)	1113 (vw)	1106 (w)	1053—1167 (w. band)
2329 (s)	2319 (m)	2313 (vw)	—

Of the five frequencies which appear in each spectrum of nitrosonium perchlorate, four may be assigned to the perchlorate ion, although, in the case of the solid, the frequency of the doubly degenerate bending vibration is considerably displaced. The fifth frequency, 2320 cm.$^{-1}$, is assigned as the fundamental frequency of the nitrosonium ion, NO^+, and this is supported by comparison with the isoelectronic molecule, N_2, which has its fundamental frequency at 2330 cm.$^{-1}$. The appearance of a line at 2320 cm.$^{-1}$ in the spectra of solutions of both nitrosonium hydrogen sulphate and the perchlorate demonstrates that the frequency is nearly independent of the remainder of the molecule, and this is consistent with its assignment to a common ion.

(1.2) *Raman Spectra of Solutions of Dinitrogen Trioxide in Sulphuric Acid.*—In Table II the frequencies belonging to three Raman spectra are given. Column 1 contains the frequencies of pure sulphuric acid (Part I, *J.*, 1950, 2576), column 2 the frequencies found in the spectrum of a mixture of 10 mols. of dinitrogen trioxide with 90 mols. of sulphuric acid, and column 3 the frequencies found in the spectrum of a solution of dinitrogen trioxide in aqueous sulphuric acid. The frequencies near 2300 cm.$^{-1}$ were measured as Raman displacements of Stokes lines excited by Hg 4047 A., an iodine filter being used. In the spectrum of the solution in anhydrous sulphuric acid, a Raman frequency of 2307·7 cm.$^{-1}$, excited as a Stokes line by Hg 4078 A., was also found. The remaining frequencies refer to measurements of Stokes lines excited by nitrite-filtered Hg 4358 A.

TABLE II.

Raman frequencies (in cm.$^{-1}$) of solutions of dinitrogen trioxide in sulphuric acid.

Pure H_2SO_4.	Solutions of N_2O_3 in (i) anhydr. H_2SO_4.	(ii) aq. H_2SO_4.	Pure H_2SO_4.	Solutions of N_2O_3 in (i) anhydr. H_2SO_4.	(ii) aq. H_2SO_4.
391 (ms) } 416 (ms) }	408 (m)	418 (m)	—	1043 (s)	1034 (vs)
562 (s)	561 (ms)	574 (m)	1125—1195 (s)	1172 (s)	1191 (ms)
912 (s)	902 (s)	903 (m)	1376 (mw)	1372 (mw)	—
976 (w)	—	—	—	1398 (vw)	—
			—	2307·9 (s)	2290 (m)

The spectrum of the solution in anhydrous sulphuric acid contains all the lines of the sulphuric acid molecule, except the weak one at 976 cm.$^{-1}$; and it contains three other lines, having the frequencies 1043, 1398, and 2307·9 cm.$^{-1}$. Two of these appear in the microphotometer record reproduced in Fig. 1.

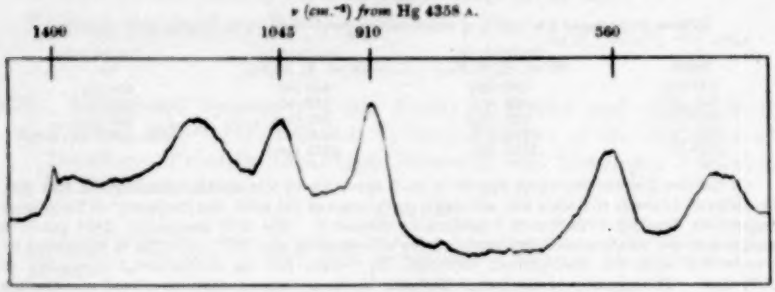
The weak frequency 1398 cm.$^{-1}$ has no significance for the ionisation of dinitrogen trioxide by sulphuric acid: it belongs to the nitronium ion. This is present as an impurity, because the heat of mixing of dinitrogen trioxide with sulphuric acid renders it difficult to prepare a mixture (cf. Gillespie *et al.*, *J.*, 1950, 2504) without causing some loss of nitric oxide, with an accompanying formation of dinitrogen tetroxide, which is the source of the nitronium ion

(cf. Section 2.2). Of the remaining frequencies, 2308 cm.$^{-1}$ and 1043 cm.$^{-1}$, the former can only be the fundamental frequency of the nitrosonium ion, whilst the latter is assigned to the hydrogen sulphate ion.

In support of this assignment of the line at 1040 cm.$^{-1}$, it may be pointed out that its contour matches that of the corresponding line in the spectrum of aqueous sulphuric acid (cf. Fig. 2b of Part I), and that those other appearances which are to be expected from the presence of the hydrogen sulphate ion are found in the spectrum. These appearances are (cf. Part I) a marked thickening and dissymmetry of the sulphuric acid line at 560 cm.$^{-1}$ in the direction of a satellite at about 590 cm.$^{-1}$, and a similar, but much smaller, deformation of the sulphuric acid line at 910 cm.$^{-1}$ in the direction of a satellite at about 895 cm.$^{-1}$ (cf. Fig. 1).

FIG. 1.

Microphotometer record of part of the Raman spectrum of a mixture of 10 *mols. of dinitrogen trioxide with* 90 *mols. of sulphuric acid.*



The spectrum of the mixture of dinitrogen trioxide and sulphuric acid is thus fully explained by assuming complete ionisation to nitrosonium ion and hydrogen sulphate ion :

$$3H_2SO_4 + N_2O_3 = 2NO^+ + 3HSO_4^- + H_3O^+$$

This equation is approximate inasmuch as it neglects the incomplete ionisation of water by sulphuric acid (Gillespie, *J.*, 1950, 2493).

It is convenient to consider the solution of dinitrogen trioxide in aqueous sulphuric acid as a mixture belonging to the system H_2SO_4–HNO_3–H_2O, and to compare its spectrum with that of the corresponding mixture of the system H_2SO_4–HNO_3–H_2O. The composition of the former system, calculated on this basis, is 43 mols. H_2SO_4, 10 mols. HNO_3, 47 mols. H_2O. The corresponding mixture in which nitric acid replaces nitrous acid contains just sufficient water to destroy all the nitronium ion (Chédin, *Ann. Chim.*, 1937, **8**, 303; Gillespie and Millen, *Quart. Reviews*, 1948, **2**, 285); and so the frequency 1400 cm.$^{-1}$ is absent from its spectrum, whilst the frequencies of molecular nitric acid are strongly developed (cf. Part I, Section 4, *J.*, 1950, 2576).

The spectrum of the mixture derived from dinitrogen trioxide shows all the characteristics of the hydrogen sulphate ion spectrum, as well as a moderately strong nitrosonium ion line near 2300 cm.$^{-1}$. Thus the spectrum can be completely understood as that of a solution of nitrosonium and hydrogen sulphate ions in sulphuric acid. There are no lines which could be attributed to an oxy-acid of nitrogen, although it is possible that weak lines might have been obscured. However, it is clear that nitrous acid exists very largely in the cationic form, NO^+, in this solution, and that nitric and nitrous acids behave in entirely different ways in the two mixtures of corresponding composition. We conclude that the equilibrium constant for the following ionisation of nitrous acid by sulphuric acid,

$$HNO_2 + 2H_2SO_4 = NO^+ + 2HSO_4^- + H_3O^+$$

is much greater than that for the corresponding ionisation of nitric acid by sulphuric acid, *viz.*,

$$HNO_3 + 2H_2SO_4 = NO_2^+ + 2HSO_4^- + H_3O^+$$

The larger negative Gibbs free-energy of formation of nitric acid than of nitrous acid, and the

reverse order of thermodynamic stability of the corresponding cations both contribute to this difference in the equilibrium constants.

(2) *Ionisation of Dinitrogen Tetroxide in Sulphuric Acid.*

(2.1) *The Condition of Dinitrogen Tetroxide in Sulphuric Acid.*—It has been shown that solutions of dinitrogen tetroxide in sulphuric acid are capable of nitrating aromatic compounds (Pinck, *J. Amer. Chem. Soc.*, **1927**, **49**, 2536). Only one nitro-group is introduced into the aromatic compound for each molecule of dinitrogen tetroxide used. If it is assumed that the effective nitrating agent in the solution is the nitronium ion, then these results are consistent with the assumption of an ionisation of dinitrogen tetroxide by sulphuric acid according to the following equation :

$$N_2O_4 + 3H_2SO_4 \rightleftharpoons NO_2^+ + NO^+ + 3HSO_4^- + H_3O^+$$

Cryoscopic examination of the solution (Gillespie *et al.*, *J.*, 1950, 2504) has yielded results which are in agreement with this equation, when a small allowance is made for the incomplete ionisation of water by sulphuric acid.

(2.2) *Raman Spectra of Solutions of Dinitrogen Tetroxide in Sulphuric Acid.*—In Table III are recorded the results of frequency measurements (cm.$^{-1}$) made upon the Raman spectra of (i) anhydrous sulphuric acid, (ii) a mixture of 10 mols. of dinitrogen tetroxide with 90 mols. of sulphuric acid, and (iii) a mixture of 20 mols. of dinitrogen tetroxide with 80 mols. of sulphuric acid. The frequencies of approximately 2300 cm.$^{-1}$ were measured as Raman displacements of Stokes lines excited by Hg 4047 A., simultaneous excitation by Hg 4358 A. being excluded by means of an iodine filter. The same frequencies were also measured as displacements, by 2302 cm.$^{-1}$, from Hg 4078 A. in the spectrum of each of the dinitrogen tetroxide solutions. The remaining frequencies refer to measurements of Stokes lines excited by nitrite-filtered Hg 4358 A.

TABLE III.

Raman frequencies (in cm.$^{-1}$) of solutions of dinitrogen tetroxide in sulphuric acid.

Pure H_2SO_4.	N_2O_4 (10 mols.) + H_2SO_4 (90 mols.).	N_2O_4 (20 mols.) + H_2SO_4 (80 mols.).	Pure H_2SO_4.	N_2O_4 (10 mols.) + H_2SO_4 (90 mols.).	N_2O_4 (20 mols.) + H_2SO_4 (80 mols.).
391 (ms) 416 (ms)	415 (ms)	412 (ms)	1125—1195 (s)	1179 (s)	1181 (s) 1313 (w)
562 (ms)	565 (ms)	565 (ms)	1376 (mw)	—	—
—	—	680 (vw)	—	1404 (s)	1400 (s)
912 (s)	903 (s)	905 (s)	—	—	1670 (vw)
976 (w)	—	—	—	2303 (s)	2301 (s)
—	1046 (s)	1042 (s)			

The spectrum of the mixture of 10 mols. of dinitrogen tetroxide with 90 mols. of sulphuric acid shows all the spectral characteristics of molecular sulphuric acid, except that the weakest frequencies, 976 cm.$^{-1}$ and 1376 cm.$^{-1}$, are not detected, and the two lowest frequencies are not resolved. In addition, three strong frequencies, of about 1045, 1400, and 2300 cm.$^{-1}$, are present. None of these has a counterpart in the Raman spectrum of dinitrogen tetroxide as observed for the solid phase (Sutherland, *Proc. Roy. Soc.*, **1933**, *A*, **141**, 342).

A microphotometer record of part of a Raman spectrum of a mixture of dinitrogen tetroxide and sulphuric acid is shown in Fig. 2. The line at 1400 cm.$^{-1}$ has the easily recognisable appearance of the nitronium ion fundamental. The line at 2300 cm.$^{-1}$ can be nothing else than the nitrosonium ion fundamental. The remaining strong frequency, 1045 cm.$^{-1}$, is assigned to the hydrogen sulphate ion. For not only has it the familiar form of the principal Raman frequency of this ion; but also those other spectral appearances which are always associated with the presence of the hydrogen sulphate ion are apparent in this spectrum.

This interpretation of the spectrum requires dinitrogen tetroxide to be ionised by sulphuric acid to produce nitrosonium, nitronium, and hydrogen sulphate ions :

$$N_2O_4 + 3H_2SO_4 \rightleftharpoons NO^+ + NO_2^+ + 3HSO_4^- + H_3O^+$$

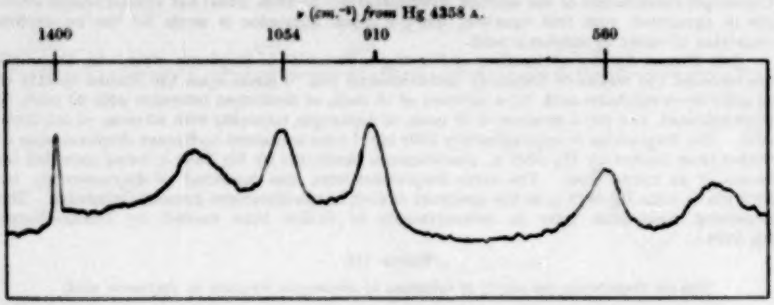
The equation is approximate, inasmuch as it neglects the incomplete ionisation of water by sulphuric acid (Gillespie, *loc. cit.*). It has been roughly confirmed by intensity measurements. Relatively to the hydrogen sulphate ion frequency 1045 cm.$^{-1}$, the nitronium ion line is approximately 1·5 times as intense in the spectra of dilute solutions of nitric acid in sulphuric acid as it is in dilute solutions of dinitrogen tetroxide in sulphuric acid. This agrees with the

chemical equations that have been given for the ionisation of nitric acid and of dinitrogen tetroxide in sulphuric acid. Even when allowance is made for the incompleteness of the ionisation of water, the intensity ratio should still be very approximately as stated.

The spectrum of a mixture of 20 mols. of dinitrogen tetroxide with 80 mols. of sulphuric acid generally resembles that of the mixture with only 10 mols. % of dinitrogen tetroxide; but there are differences. The increase in concentration of the tetroxide has resulted in an increase in intensity, relative to the molecular sulphuric acid lines, of the characteristic lines of the hydrogen sulphate ion, the nitrosonium ion, and the nitronium ion. Furthermore, three weak lines are present, which were not found in the spectrum of the more dilute solution of

FIG. 2.

Microphotometer record of part of the Raman spectrum of a mixture of 10 *mols. of dinitrogen tetroxide with* 90 *mols. of sulphuric acid.*



dinitrogen tetroxide. The appearance of these frequencies, 680, 1313, and 1670 cm.$^{-1}$, is attributed to the presence of molecular nitric acid in the mixture. A careful consideration of the known spectra of nitric acid, and its mixtures with sulphuric acid (Part I, *J.*, 1950, 2576), supports the view that the three lines actually have this origin. Evidently the concentrations of nitronium, hydroxonium, and hydrogen sulphate ions have reached such magnitude that a spectroscopically detectable quantity of molecular nitric acid is formed, according to the equation

$$NO_2^+ + 2HSO_4^- + H_3O^+ \rightleftharpoons HNO_3 + 2H_2SO_4$$

(3) *Ionisation of Dinitrogen Pentoxide by Sulphuric Acid.*

(3.1) *The Condition of Dinitrogen Pentoxide in Sulphuric Acid.*—Klemenc and Schöller showed (*Z. anorg. Chem.*, 1924, **141**, 231) that solutions of dinitrogen pentoxide in sulphuric acid are very effective nitrating agents, having nitrating properties closely similar to those of solutions of nitric acid in sulphuric acid. They also showed that rate of nitration by a solution of dinitrogen pentoxide is equal to that by a solution of twice as many molecules of nitric acid. These observations are consistent with assumed ionisation of dinitrogen pentoxide and nitric acid by sulphuric acid according to the following equations:

$$N_2O_5 + 3H_2SO_4 = 2NO_2^+ + 3HSO_4^- + H_3O^+$$
$$HNO_3 + 2H_2SO_4 = NO_2^+ + 2HSO_4^- + H_3O^+$$

(3.2) *Raman Spectra of Solutions of Dinitrogen Pentoxide in Sulphuric Acid.*—Table IV contains the results of frequency measurements made on the Raman spectra of sulphuric acid, and of two solutions of dinitrogen pentoxide in sulphuric acid. The recorded frequency displacements (cm.$^{-1}$) were all measured on Stokes lines excited by nitrite-filtered Hg 4358 A.

The spectrum of the more dilute solution of dinitrogen pentoxide in sulphuric acid contains all the characteristic lines of the sulphuric acid molecule, except the two weak ones at 976 cm.$^{-1}$ and 1376 cm.$^{-1}$. It contains in addition two strong lines, one at 1045 cm.$^{-1}$ and the other at 1400 cm.$^{-1}$. The spectrum is, in fact, qualitatively similar to those obtained for solutions of nitric acid in sulphuric acid.

The microphotometric record of the spectrum, reproduced in Fig. 3, shows the now familiar

character of the ionic lines at 1400 and 1045 cm.$^{-1}$. There can be no doubt that they belong to the nitronium ion, and the hydrogen sulphate ion, respectively. We also see in the spectrum those other appearances which indicate the presence of the hydrogen sulphate ion, *viz.*, the strong dissymmetry of the line at 560 cm.$^{-1}$, and the oppositely directed and weaker dissymmetry of the line at 910 cm.$^{-1}$.

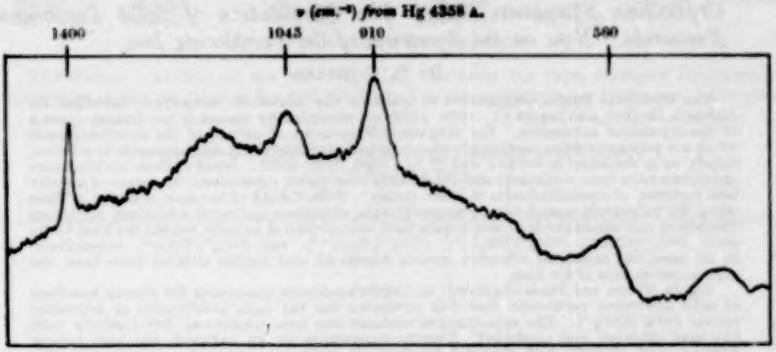
TABLE IV.

Raman frequencies of solutions of dinitrogen pentoxide in sulphuric acid.

Pure H_2SO_4.	N_2O_5 (10 mols.) + H_2SO_4 (90 mols.).	N_2O_5 (30 mols.) + H_2SO_4 (70 mols.).	Pure H_2SO_4.	N_2O_5 (10 mols.) + H_2SO_4 (90 mols.).	N_2O_5 (30 mols.) + H_2SO_4 (70 mols.).
391 (ms) 416 (ms)	403 (ms)	407 (ms)	—	1046 (ms)	1044 (s)
562 (ms)	565 (ms)	567 (ms)	1125—1195 (s)	1160 (s)	1175 (ms)
—	—	610 (w)	—	—	1315 (ms)
—	—	677 (w)	1376 (mw)	—	—
912 (s)	910 (s)	907 (s)	—	1401 (ms)	1402 (s)
976 (w)	—	—	—	—	1673 (w)

FIG. 3.

Microphotometer record of part of the Raman spectrum of a mixture of 10 mols. of dinitrogen pentoxide with 90 mols. of sulphuric acid.



These results show that dinitrogen pentoxide is ionised in sulphuric acid according to the approximate equation

$$N_2O_5 + 3H_2SO_4 = 2NO_2^+ + 3HSO_4^- + H_3O^+$$

which disregards the incompleteness of the ionisation of water in sulphuric acid (Gillespie, *loc. cit.*).

Some intensity measurements have been made, which agree with this representation. The ratio of the intensity of the nitronium ion line at 1400 cm.$^{-1}$ to that of the hydrogen sulphate ion line at 1045 cm.$^{-1}$ in spectra of dilute solutions of dinitrogen pentoxide in sulphuric acid, is approximately twice the corresponding ratio for spectra of dilute solutions of dinitrogen tetroxide in sulphuric acid. This is evidently consistent with equations we have written to represent the relevant ionisations.

The spectrum of the mixture of 30 mols. of dinitrogen pentoxide with 70 mols. of sulphuric acid is more complicated than that of the more dilute solution. It contains lines corresponding to all those in the spectrum of the more dilute solution; but the intensities of the lines due to the nitronium and hydrogen sulphate ions are increased relative to the intensities of the molecular sulphuric acid lines. In addition, four lines, which have frequencies of 610, 677, 1315, and 1673 cm.$^{-1}$, are visible. There can be no doubt that these lines are four of the five strongest Raman lines of molecular nitric acid. This is shown by comparisons of both the frequencies and the relative intensities with those observed in the Raman spectra of nitric acid and its mixtures with sulphuric acid (cf. Table II of Part I, *J.*, 1950, 2576). The fifth of the

strong, or moderately strong, Raman fundamentals of nitric acid, 925 cm.$^{-1}$, is expected to be visible here only as a deflexion of the contour of the sulphuric acid line at 910 cm.$^{-1}$; such a deflexion is, indeed, observed.

From the evidence it follows that, in the solution containing 30 mols. % of dinitrogen pentoxide, the concentrations of nitronium and hydrogen sulphate ions have reached such values that appreciable quantities of molecular nitric acid are formed by the balanced reaction,

$$NO_2^+ + H_3O^+ + 2HSO_4^- \rightleftharpoons HNO_3 + 2H_2SO_4$$

In other words, the ionic dehydration of dinitrogen pentoxide to the nitronium ion in sulphuric acid can, with an adequate supply of the pentoxide, proceed so far as to produce ionised water in sufficient concentration to rehydrate some of the dinitrogen pentoxide to nitric acid, even in the presence of sulphuric acid.

The author is indebted to Professor C. K. Ingold, F.R.S., for invaluable help and encouragement.

William Ramsay and Ralph Forster Laboratories,
University College, London, W.C.1. [*Received, December 17th*, 1949.]

---

509. *Vibrational Spectra of Ionic Forms of Oxides and Oxy-acids of Nitrogen. Part IV. Raman Spectral Evidence of Ionisation in Crystalline Nitronium Salts. The Constitution of Solid Dinitrogen Pentoxide. Note on the Spectrum of the Perchlorate Ion.*

By D. J. Millen.

The structural lattice components of some of the nitronium compounds described by Goddard, Hughes, and Ingold (*J.*, 1950, 2559) are identified by means of the Raman spectra of the crystalline substances. The diagnostic frequencies of certain of the structural units which are present in these compounds were originally established by measurements in solution, largely as is described in Parts I and II (*J.*, 1950, 2576, 2589). Some of these identification characters have been confirmed, and others have been newly determined, by means of a study here reported, of crystalline salts of alkali metals. With the aid of the data obtained in these ways, the substances named nitronium perchlorate, nitronium hydrogen disulphate, nitronium disulphate, and nitronium fluorosulphonate have been proved to be salts, having the ionic structures $(NO_2^+)(ClO_4^-)$, $(NO_2^+)(HS_2O_7^-)$, $(NO_2^+)_2(S_2O_7^{--})$, and $(NO_2^+)(FSO_3^-)$, respectively. In all cases, the molecular vibration spectra consist of, and display nothing more than, the superposed spectra of the ions.

Ingold, Millen, and Poole concluded, on Chédin's evidence concerning the Raman spectrum of solid dinitrogen pentoxide, that this substance has the ionic constitution of nitronium nitrate $(NO_2^+)(NO_3^-)$. The experimental evidence has been questioned, but Chédin's work has been repeated and confirmed. Despite suggestions to the contrary, the high vapour pressure, and allegedly high chemical constant, of dinitrogen pentoxide are not necessarily difficulties in relation to its ionic constitution.

Incidentally to this work, an obscure point concerning the vibration frequencies of the perchlorate ion is cleared up.

(1) *Raman Spectra of Crystalline Nitronium Salts.*

(1.1) *Scope of this Work.*—In accompanying papers, physical evidence of various kinds has been provided for the ionisation of nitric acid by certain very strong acids. It has been shown that the products of ionisation of nitric acid by a strong acid HX include the nitronium ion NO_2^+ and the anion X^-. The isolation of certain solid products, which involve the ionisation of nitric acid in this manner, has been described by Goddard, Hughes, and Ingold (*J.*, 1950, 2559). Some of these solids have compositions corresponding to the general formula NO_2X.

The present paper describes the identification of the crystalline-lattice components of some solids isolated by these authors. In addition, solid dinitrogen pentoxide, which is the member of the series NO_2X with $X = NO_3$, has been re-examined. The method of investigation was Raman spectroscopy, by which the structural units of the crystals were identified from their known spectra. The diagnostic characteristics of some of these constituents have been established in Parts I and II. The identification of a number of the constituents was confirmed by a special study of the Raman spectra of certain comparison substances.

(1.2) *Solids derived from the System* HNO_3–$HClO_4$.—Goddard, Hughes, and Ingold obtained two solid materials of definite composition from this system. One of these corresponded to the formula $NClO_4$, and the other to $H_2NCl_3O_{11}$. It was important to establish the nature of

the compounds, since the structure of the second had been claimed to be $(H_2NO_3^{++})(ClO_4^-)_2$, in support of the view that the ionisation of nitric acid in strong acids produces the ion $H_2NO_3^{++}$.

The frequencies observed in the Raman spectra of these two solids are recorded in Table I, together with the frequencies of the perchlorate ion as observed in an aqueous solution of sodium perchlorate (Redlich, Holt, and Bigeleisen, *J. Amer. Chem. Soc.*, 1944, **66**, 13). All the frequencies of the two solids were observed as Stokes lines excited by nitrite-filtered Hg 4358 A. A microphotometer trace of part of the spectrum of $NClO_4$ is reproduced in Fig. 1.

It is evident from Table I that the Raman spectrum of solid $NClO_4$ consists simply of the superposed Raman spectra of the perchlorate and nitronium ions. (The reason for the observation of a doublet in place of a band is considered in Section 3.) This establishes that, as was first reported in a preliminary note (*Nature*, 1946, **158**, 480), the solid has the ionic structure $(NO_2^+)(ClO_4^-)$. The crystal structure of this substance has also been investigated by *X*-ray methods (Cox, Jeffery, and Truter, *Nature*, 1948, **162**, 259), with results which confirm the assigned constitution.

TABLE I.

Raman frequencies (cm.$^{-1}$) of crystalline solids derived from the system HNO_3–$HClO_4$. *Comparison with the Raman frequencies of the perchlorate ion.*

Solid $NClO_4$.	Solid $H_3NCl_2O_{11}$.	ClO_4^- ion (R., H., and B.).	Solid $NClO_4$.	Solid $H_3NCl_2O_{11}$.	ClO_4^- ion (R., H., and B.).
461 (mw)	460 (mw)	461 (m)	1082 (mw)	—	1058 to 1167 (w, band)
626 (m)	625 (m)	631 (ms)	1143 (mw)	—	
937·8 (vs)	926 (s)	940 (vs)	1396·2 (vs) *	1395·4 (s) *	—

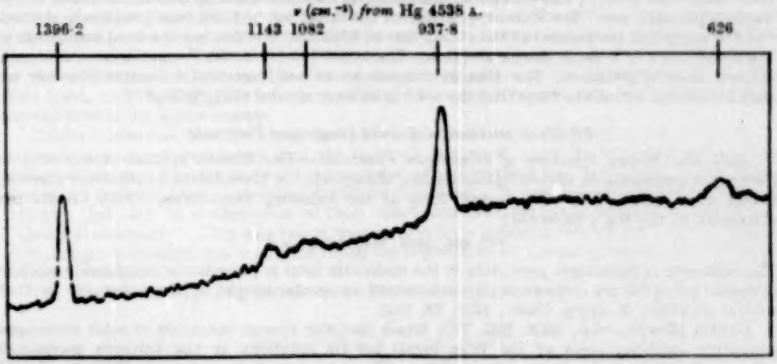
* Nitronium ion frequency.

The Raman spectrum of the solid $H_3NCl_2O_{11}$ contains the three strongest fundamental frequencies of the perchlorate ion and the Raman-active nitronium ion frequency. The solid

FIG. 1.

Microphotometer trace of part of the Raman spectrum of solid $NClO_4$.

ν (cm.$^{-1}$) *from* Hg 4538 A.



must therefore contain the nitronium and perchlorate ions. Its composition can be explained by supposing it to be a mixture of nitronium perchlorate and the well-known monohydrate of perchloric acid in equimolecular proportions. The monohydrate doubtless has the ionic constitution $(H_3O^+)(ClO_4^-)$. Its Raman spectrum is simply that of the perchlorate ion, since, as is well known, the hydroxonium ion does not give a distinct Raman spectrum.* For stoicheiometric reasons the two substances $(NO_2^+)(ClO_4^-)$ and $(H_3O^+)(ClO_4^-)$ are necessarily produced from nitric and perchloric acids in equimolecular proportions, and some of the preparative methods which have been employed leave little opportunity for even partial separation.

* Further attempts will be made to find a hydroxonium ion spectrum in solid hydroxonium perchlorate; but all that can be seen on the Raman spectrograms so far secured is the perchlorate ion spectrum.

(1.3) *Solids derived from the System* N_2O_5–SO_3–H_2O.—Two of the solid phases that Goddard, Hughes, and Ingold obtained from this system have been examined spectroscopically. They have compositions corresponding to the formulæ $(NO_2)HS_2O_7$ and $(NO_2)_2S_2O_7$. The spectral characteristics of the anions $HS_2O_7^-$ and $S_2O_7^{--}$ were considered in Part II (*J.*, 1950, 2589) on the basis of a study of the Raman spectra of solutions in sulphuric oleum. In order to confirm the conclusions thus derived and to establish a sound basis for the spectroscopic identification of these anions, solid potassium disulphate $K_2S_2O_7$, and solid potassium hydrogen disulphate KHS_2O_7, have now been examined. The results obtained for both the nitronium salts and the reference potassium salts are assembled in Table II. These frequencies were measured as Stokes lines excited by Hg 4358 A. Only the strongest Raman frequencies of the hydrogen disulphate and normal disulphate ions are recorded clearly enough for measurement in the spectra of the solid salts.

It is obvious from Table II that the two nitrogen compounds are nitronium hydrogen disulphate $(NO_2^+)(HS_2O_7^-)$ and nitronium disulphate $(NO_2^+)_2(S_2O_7^{--})$. Their Raman frequencies correspond to those of potassium hydrogen disulphate and potassium disulphate, respectively, except for the additional frequency, 1400 cm.$^{-1}$, given by the former pair of compounds, which is evidently due to the nitronium ion.

TABLE II.

Raman frequencies (cm.$^{-1}$) of solid potassium and nitronium salts derived from disulphuric acid.

$(NO_2)HS_2O_7$.	$(NO_2)_2S_2O_7$.	KHS_2O_7.	$K_2S_2O_7$.
1075	1096	1073	1096
1396 *	1401 *	—	—

* Nitronium ion frequency.

(1.4) *Solid derived from the System* N_2O_5–$F{\cdot}SO_3H$.—In the Raman spectrum of this solid substance which has the composition $(NO_2)FSO_3$, strong sharp lines were observed at 1405 cm.$^{-1}$ and 1083 cm.$^{-1}$. The former is attributed to the nitronium ion, and the latter to the fluorosulphonate ion. The Raman spectrum of the latter ion had not been previously studied, but the suggested assignment of the strong line at 1083 cm.$^{-1}$ to this ion has been confirmed by the observation of a single strong and sharp line at 1087 cm.$^{-1}$ in the Raman spectrum of solid lithium fluorosulphonate. The Raman frequencies of solid nitronium fluorosulphonate are thus accounted for on the basis that the solid is an ionic crystal $(NO_2^+)(SO_3F^-)$.

(2) *The Constitution of Solid Dinitrogen Pentoxide.*

(2.1) *The Raman Spectrum of Dinitrogen Pentoxide.*—The Raman spectra of solutions of dinitrogen pentoxide in carbon tetrachloride, chloroform, or phosphorus oxychloride (Chédin, *Compt. rend.*, 1935, **201**, 552) contain lines at the following frequencies, which Chédin has attributed to the N_2O_5 molecule:

707, 860, 1033, 1240, 1335 cm.$^{-1}$

The existence of dinitrogen pentoxide in the molecular form in phosphorus oxychloride solution is consistent with the cryoscopically determined molecular weight of the substance in that solvent (Walden, *Z. anorg. Chem.*, 1910, **68**, 314).

Chédin (*Compt. rend.*, 1936, **203**, 722) found that the Raman spectrum of solid dinitrogen pentoxide contains none of the lines found for its solutions in the solvents mentioned above. Instead, there appeared two sharp lines having frequencies of 1051 cm.$^{-1}$ and 1400 cm.$^{-1}$. Chédin accounted for these spectral differences by supposing that dinitrogen pentoxide exists in the solid state, not in the molecular form, but in some modified form. This modified form has been interpreted by Ingold, Millen, and Poole (*Nature*, 1946, **158**, 480) as the ionic form $(NO_2^+)(NO_3^-)$. They assigned the frequency of 1400 cm.$^{-1}$ to the nitronium ion, and the frequency 1050 cm.$^{-1}$ to the nitrate ion, and supposed that the other two fundamental frequencies of the nitrate ion were not observed in the spectrum of the solid because of their low intensity compared with that of the frequency of 1050 cm.$^{-1}$ (cf. Part V, *J.*, 1950, paper no. 510).

An alternative explanation of the origin of the lines at 1050 cm.$^{-1}$ and 1400 cm.$^{-1}$ in the Raman spectrum of the solid has, however, been suggested in certain widely circulated documents. This is that small quantities of nitric acid might have been present among the crystals Chédin employed, and that dinitrogen pentoxide, although covalent in the solid state, dissolved and

ionised in this nitric acid to produce nitronium and nitrate ions. The Raman spectrum of a solution of these ions in nitric acid does contain sharp lines at 1050 cm.$^{-1}$ and 1400 cm.$^{-1}$, as has been directly observed (cf. Part V). This explanation is, however, not satisfactory, because none of the lines of molecular nitric acid was observed by Chédin in the spectrum.

In order to establish conclusively which of these interpretations is correct, the observation of the Raman spectrum of solid dinitrogen pentoxide has been repeated, under conditions which ensure the absence of nitric acid from the crystals. Dinitrogen pentoxide was distilled in a stream of ozonised oxygen on to phosphoric oxide, and redistilled through phosphoric oxide into a Raman cell. The cell was then closed by ground-glass caps which were externally sealed with metaphosphoric acid. The spectroscopic result confirms that of Chédin: the spectrum of the solid at −40° contains sharp lines at 1047 cm.$^{-1}$ and 1394 cm.$^{-1}$, and naturally no vestige of any lines of molecular nitric acid.

All the collateral evidence in this paper shows that the Raman-spectral method is a valid one for identifying the structural units in crystals. The constitution of nitronium perchlorate, which was first established in this way, has since been confirmed by *X*-ray methods (Cox, Jeffery, and Truter, *loc. cit.*). It is therefore impossible to escape the conclusion * that solid dinitrogen pentoxide has the ionic structure $(NO_2^+)(NO_3^-)$, just as solid phosphorus pentachloride has the ionic structure $(PCl_4^+)(PCl_6^-)$. In the vapour phase the anhydride consists of N_2O_5 molecules, just as sodium chloride vapour consists essentially of NaCl molecules.

(2.2) *The Volatility of Dinitrogen Pentoxide.*—We are accustomed to regarding low volatility as one of the characteristics of ionic crystalline substances. Dinitrogen pentoxide has, however, a sublimation pressure of approximately 200 mm. at 15°. The comparatively high volatility of dinitrogen pentoxide is connected with its low latent heat of sublimation in comparison with the latent heats of the majority of ionic crystals. Whereas the latent heats of sublimation of the alkali chlorides are of the order of 50 kcals./g.-mol., the latent heat for dinitrogen pentoxide is approximately 13 kcals./g.-mol. (Russ and Pokorny, *Monatsh.*, 1913, **34**, 1040; Daniels and Bright, *J. Amer. Chem. Soc.*, 1920, **42**, 1131). The energy required for the vaporisation of an ionic crystal depends upon the difference between the lattice energy of the crystal and the energy obtained from the pairing of the ions to form the gaseous molecules. In the case of sodium chloride, for instance, the high value of the lattice energy (about 180 kcals./g.-mol.), and the considerably smaller energy of formation of sodium chloride molecules from Na^+ and Cl^- ions (about 125 kcals./g.-mol.), results in a large latent heat of sublimation. In the sublimation of dinitrogen pentoxide, the energy gained in the formation of a covalent N–O bond, and the consequent electron redistribution, much more nearly compensates for the expenditure of the lattice energy.

Chédin's inference that the dinitrogen pentoxide molecule is modified in the solid state is particularised in our conclusion that the molecule is ionised; but the opposite form of particularisation, *viz.*, that the molecule is associated or polymerised, has been made, and has been quoted, so that the basis of the idea should be examined. It was first advanced by Russ and Pokorny (*loc. cit.*), in consequence of their conclusion that dinitrogen pentoxide has a high "chemical constant." This conclusion was derived by a consideration of the vapour pressure of dinitrogen pentoxide, the connexion being the dependence of vapour pressure on the vapour-pressure constant.

The equilibrium vapour pressure of a solid at a temperature T is given by the equation

$$\ln p = -\frac{L_0}{RT} + \int_0^T \frac{dT}{RT^2} \int_0^T \Delta C_p dT + i$$

provided that we may assume the vapour to behave as an ideal gas. Here L_0 is the molar heat of sublimation at the absolute zero of temperature, ΔC_p is the difference between the heat capacities of the two phases ($\Delta C_p = C_{p(\text{gas})} - C_{p(\text{solid})}$), and i is the vapour-pressure constant of the substance. Thus a high vapour pressure may arise either from a low latent heat of sublimation, or from a high vapour-pressure constant, or (except at low temperatures) from a high heat-capacity difference; or, of course, from any combination of these causes.

* [*Added in proof*, 14.7.50.] A very recent paper by Grison, Ericks, and de Vries (*Acta Cryst.*, 1950, **3**, 290) gives *X*-ray confirmation of the ionic structure, together with the complete crystal geometry. The linear centrosymmetric NO_2^+ ions lie normal to the planes of the trigonal planar NO_3^- ions. The bond-length of the NO_2^+ ion, 1·156 ± 0·01 A., is the most accurate yet recorded. It is of interest to compare it with the spectroscopically measured bond-length of carbon dioxide, *viz.*, 1·163 A., and with the *X*-ray bond-length of the ion N_3^-, viz., 1·15 ± 0·02 or 1·165 ± 0·02 A.

The constant i is connected with other thermodynamic functions through the equation

$$i = (\Delta S^\circ - C^\circ_{p(gas)})/R$$

where ΔS° is the difference between the molar entropies of the phases at the zero of temperature ($\Delta S^\circ = S^\circ_{(gas)} - S^\circ_{(solid)}$), and $C^\circ_{p(gas)}$ is the molar heat capacity of the vapour at the zero of temperature. The conditions for a high value of i are therefore a high entropy for the vapour and a low entropy for the solid. The following conditions are some of those which would contribute to such a situation: (1) no disorder in the solid at the absolute zero of temperature; (2) no degeneracy in the ground state of the solid; (3) a molecular symmetry number equal to unity; (4) degeneracy in the ground state of the gaseous molecule. If we assume that orientation in the crystal at the absolute zero of temperature is perfect, that there is no degeneracy in either the solid or the gas, and that the symmetry number of the non-linear gaseous molecule is unity (so that all rotational states are available), then i is given by the equation

$$i = \ln (64\pi^4 k^4 m^{3/2} (ABC)^{1/2}/h^3)$$

where m is the mass, and A, B, and C are the principal moments of inertia, of the gaseous molecule, k is Boltzmann's constant, and h is Planck's constant. Unfortunately, we do not know enough about the molecular dimensions of dinitrogen pentoxide to obtain a good value of i from this equation; but there seems to be no reason to suspect an abnormally high value. The same statement could be made if the symmetry number were two, as it might be.

The other possible method of obtaining i involves the use of the integrated vapour-pressure equation given above. However, the application of this method to dinitrogen pentoxide would require much more knowledge than we possess of the specific heat of this substance. For the vapour, at temperatures at which vibration is unexcited, we might make the approximation, $C_{p(gas)} = C^\circ_{p(gas)}$, which amounts to assuming that rotation is classical down to the temperature zero. But still $C_{p(solid)}$ will vary in a complicated way, owing to the acoustical vibrations in the crystal lattice. Yet, without a knowledge of ΔC_p as a function of temperature, it is impossible to deduce i from the temperature variation of $\ln p$.

Now Russ and Pokorny obtained their constant, which they called the "chemical constant," by the use of an empirical vapour-pressure equation. This was in 1913, before much was known about the third law, or, for that matter, about the variation of specific heats of solids with temperature. Their constant is really no more than the temperature-independent term in their particular empirical equation. At that time, it appeared that constants so obtained were approximately the same for most substances. But water had a high "chemical constant"; and this seems to have led to the assumption that associated substances had high chemical constants. That is how the idea originated that solid dinitrogen pentoxide is associated.

(3) *Note on the Raman Spectrum of the Perchlorate Ion.*

(3.1) *The Five Raman Frequencies of the Perchlorate Ion in Crystals.*—In Section 1.2, five of the Raman frequencies of crystalline nitronium perchlorate were assigned to the perchlorate ion. A regular tetrahedral structure for the perchlorate ion requires that it should possess four fundamental vibration frequencies, all of which should be active in the Raman spectrum. The observation of the Raman spectra of aqueous solutions of perchlorates (Redlich, Holt, and Bigeleisen, *loc. cit.*) has established the existence of fundamental frequencies of approximately 460 (m), 630 (ms), and 935 (vs) cm.$^{-1}$. A fourth frequency has generally been reported as a broad, weak band extending approximately from 1050 to 1170 cm.$^{-1}$. In the Raman spectrum of solid nitronium perchlorate there appear two lines, at 1080 and 1143 cm.$^{-1}$, instead of the usual broad band. The resolution of these two lines is clearly shown on the microphotometer record reproduced in Fig. 1.

TABLE III.

Raman displacements (cm.$^{-1}$) of Stokes lines excited by Hg 4358 A. *in the spectra of some solid perchlorates.*

$KClO_4$	461 (mw)	628 (m)	938 (vs)	1073 (mw)	1121 (mw)	—	
$NClO_4$	461 (mw)	626 (m)	938 (vs)	1082 (mw)	1143 (mw)	1396 (s) *	

* Nitronium ion line.

Previous records of the Raman spectrum of crystalline potassium perchlorate include no mention of a frequency near 1100 cm.$^{-1}$, and the Raman spectrum of this crystal has therefore been re-examined. Again five Raman lines, which necessarily must belong to the perchlorate

ion, have been found, including two in the neighbourhood of 1100 cm.$^{-1}$. The comparison in Table III of the observed frequencies of potassium and nitronium perchlorates leaves no doubt that the perchlorate ion possesses five Raman frequencies. It is accordingly necessary to consider the assignment of these frequencies.

(3.2) *Assignment of Frequencies of the Perchlorate Ion.*—The normal vibrations of a regular tetrahedral molecule XY_4 are classified according to their symmetry in Table IV. The 9 degrees of vibrational freedom are distributed over one non-degenerate, one doubly degenerate, and two triply degenerate vibrations. An assignment of frequencies of the perchlorate ion to these vibrations is indicated on the right-hand side of the Table.

It is certain that the intense Raman frequency 935 cm.$^{-1}$ belongs to the "breathing" vibration ν_1. It is equally definite that the two low frequencies, 630 and 460 cm.$^{-1}$, collectively belong to the bending vibrations ν_2 and ν_4. Redlich, Holt, and Bigeleisen (*loc. cit.*) have assigned these two frequencies in the manner indicated in the Table, on the basis of a comparison with the spectrum of perchloric acid. This particular allocation of the frequencies may be regarded as probably, but not certainly, correct. However, even if the assignments of these two frequencies should have to be interchanged,* it would make no difference to the following discussion of the remaining two observed frequencies, and of the remaining normal vibration ν_3.

The present suggestion is that the observed doublets near 1100 cm.$^{-1}$ in the solid perchlorates constitute the simplest type of result that can arise from Fermi resonance between the fundamental frequency ν_3 and the combination tone $\nu_1 + \nu_4$. The fundamental vibration has symmetry F_2 (Table IV). The combination state consists of two sub-states, degenerate in themselves and with each other, one of symmetry F_1,† and the other of symmetry F_2. The

TABLE IV.

Normal vibrations of regular tetrahedral molecules XY_4.

Vibration.	Symmetry.	Deg. of freedom.	Approximate description.	ClO_4^- (cm.$^{-1}$).
ν_1	A_1	1	Totally symmetrical; synchronous stretching.	935
ν_2	E	2	Doubly degenerate; bending; external atoms converge in pairs synchronously.	630
ν_3	F_2	3	Triply degenerate; stretching; external atoms displaced towards a common but indefinite direction.	~1110 *
ν_4	F_2	3	Triply degenerate; bending; external atoms bent towards a common but indefinite direction.	460

* Split by Fermi resonance—see text.

former is forbidden in the Raman effect, but the latter is allowed, and is of the right symmetry for resonance with the fundamental vibration. The unperturbed frequency of the combination tone would be 1090 cm.$^{-1}$, and it is assumed that this is close enough to the unperturbed fundamental frequency, ν_3, estimated as approximately 1110 cm.$^{-1}$, to permit resonance under the coupling action of anharmonicity. The result is a further separation of the frequencies, and a sharing of the intensities, so that one observes a doublet.

(3.3) *Nature of the Raman Band around* 1100 *cm.*$^{-1}$ *of the Perchlorate Ion in Solution.*—It has now to be considered why the Raman doublet of the perchlorate ion in the crystal becomes replaced by a diffuse band in observations on the perchlorate ion in solution. The evident cause is the high degeneracy of the vibrational states concerned. Contributing to the Fermi doublets there are really six vibrational energy states, arranged, according to the preceding discussion, in two sets of three, *i.e.*, in two levels. However, strict degeneracy within each set of three will be preserved only so long as the equilibrium configuration about which the ion is vibrating has the full symmetry of a regular tetrahedron. Since ions can never be obtained in practical concentrations otherwise than under the influence of strong external fields, this condition will be fulfilled or approached only if such external fields have a high degree of symmetry. The field acting on an individual perchlorate ion in a crystal will always have a large amount of symmetry, and in some crystals at least it may be so symmetrical as to cause no serious breakdown of the degeneracies. These are the conditions in which we

* [*Added in proof*, 14.7.50.] They have, indeed, to be interchanged; Mr. H. Cohn has found the frequency 630 cm.$^{-1}$ in the infra-red spectra of solid nitronium and metal perchlorates. This shows that it is ν_4, so that 460 cm.$^{-1}$ must be ν_2. These observations are so recent that the text above has not been altered.

† The symmetry F_1 may be described as that of an isotropic rotation, just as the symmetry F_2 is that of an isotropic translation (cf. Table IV).

observe the Fermi doublets. In aqueous solution, however, any ion which does not form a stereochemically stable polyhydrate will always be under strongly dissymmetric forces. This should cause the six energy states of the Fermi doublet to fall apart, so that instead of two levels, we shall have six levels. Furthermore, the dissymmetric forces are not steady, but are fluctuating with the thermal motion. One can readily understand how, in these circumstances, the comparable intensities of six diffuse and overlapping Raman lines integrate to the intensity distribution of a broad band, extending, according to the observations, over more than 100 cm.$^{-1}$.

The author is indebted to Professor C. K. Ingold, F.R.S., for continued encouragement and advice.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, December 17th*, 1949.]

---

510. *Vibrational Spectra of Ionic Forms of Oxides and Oxy-acids of Nitrogen. Part V. Raman Spectral Evidence of the Ionisation of Dinitrogen Pentoxide in Nitric Acid, and of the Constitution of Anhydrous Nitric Acid.*

By C. K. INGOLD and D. J. MILLEN.

With the aid of previous, and of some new, observations, the Raman spectra of nitric acid and of the nitrate ion are considered, separately and in combination; and the conclusions are used in order to interpret spectral evidence concerning the condition of dinitrogen pentoxide in nitric acid, and the self-dissociation of nitric acid.

The vibrational assignment of observed bands in the Raman and infra-red spectra of nitric acid has been completed. The key to the problem is the Raman line at 1535 cm.$^{-1}$. It is assigned as the first overtone, by which the out-of-plane vibration of the NO_2 group is expected to be more strongly represented in the Raman spectrum than by its fundamental frequency. This agrees with the polarisation, and the lack of a hydrogen-isotope shift, of the line, and with the existence in the infra-red, but not in the Raman, spectrum, of the corresponding fundamental frequency. This decided, all other details of these spectra fall easily into place. The three chief Raman frequencies of the nitrate ion have an agreed assignment to the three planar fundamentals of the ion; and the fourth observed Raman frequency, 1665 cm.$^{-1}$, is again assigned as the first overtone of the out-of-plane vibration, the fundamental frequency of which should occur, and is known, in the infra-red. The nitrate ion, when present to the extent of some units % in nitric acid, can be recognised indubitably by its Raman spectrum.

In the Raman spectrum of dinitrogen pentoxide in solution in nitric acid, the nitronium ion and the nitrate ion are completely identified; and their spectra are shown to account for the whole of the solute. No trace of the known spectrum of the covalent dinitrogen pentoxide molecule is found. It is concluded that dinitrogen pentoxide is a strong electrolyte in nitric acid, the ions of the dissolving solid falling apart without covalency change, as when sodium chloride dissolves in water. Analytically anhydrous nitric acid is shown by its Raman spectrum to contain about 2·5% of dinitrogen pentoxide and 0·5% of water—estimates which are in satisfactory agreement with those determined cryoscopically (*J.*, 1950, 2552).

(I) *Raman Spectrum of Nitric Acid.*

(1.1) *General Survey of Frequency Assignments.*—For the purposes of the analyses given later in this paper, it will be necessary to have arrived at a complete understanding of those Raman frequencies of nitric acid which belong to the molecular form of the acid.

The Raman spectrum of nitric acid has been described by a number of investigators. There is general agreement as to the main frequencies which are given below in cm.$^{-1}$, along with the usual qualitative indications of intensity (cf. Part I). The frequencies belonging to molecular nitric acid, whose assignment to vibrations is first to be discussed, are in the first row. The two frequencies in the second row do not belong to molecular nitric acid:

610 (ms)	680 (ms)	925 (s)	1300 (vs)	1535 (w)	1675 (m)	3400 (band)
		1050 (w)		1400 (w, sharp)		

(Rao, *Nature*, 1929, **124**, 762; *Proc. Amsterdam Acad.*, 1930, **33**, 632; *Proc. Roy. Soc.*, 1931, *A*, **127**, 279; Woodward, *Nature*, 1930, **58**, 126; *Physikal. Z.*, 1931, **32**, 212; Kinsey, *Physical Rev.*, 1930, **35**, 284; Dadieu and Kohlrausch, *Naturwiss.*, 1931, **19**, 690; Dadieu, Jele, and Kohlrausch, *Monatsh.*, 1931, **58**, 428; Médard and Volkringer, *Compt. rend.*, 1933, **197**, 833; Médard and Petitpas, *ibid.*, p. 1221; 1934, **198**, 98; Médard, *ibid.*, p. 1407; Aderhold and Weiss, *Z. Physik*, 1934, **88**, 83; Angus and Leckie, *Nature*, 1934, **134**, 572; *Proc. Roy. Soc.*,

1935, *A*, **149**, 327; Susz and Briner, *Helv. Chim. Acta*, 1935, **18**, 379; Venkateswaran, *Proc. Indian Acad. Sci.*, 1936, *A*, **4**, 174; Chédin, *Ann. Chim.*, 1937, **8**, 243; *J. Phys. Radium*, 1939, **10**, 445; Simon and Hoppner, *Kolloid Z.*, 1938, **85**, 8; Chédin and Delmon, *Compt. rend.*, 1939, **209**, 455; Banerji and Mishra, *Indian J. Physics*, 1941, **15**, 359; Mathieu and Massignon, *Compt. rend.*, 1941, **212**, 1084; *Ann. Physique*, 1941, **16**, 5; Redlich and Nielsen, *J. Amer. Chem. Soc.*, 1943, **65**, 654; Chédin and Fénéant, *Mem. Serv. Chim. de l'État*, 1945, **32**, 92).

Measurements of, or qualitative observations on, the polarisation of the Raman lines have been made (in some cases using more or less aqueous nitric acid) by Venkateswaran, by Chédin, and by Mathieu and Massignon (*locc. cit.*). Of the frequencies in the first row of the above list, 680, 925, 1300, and 1535 cm.$^{-1}$ are definitely polarised, whilst 610 and 1675 cm.$^{-1}$ are classified as depolarised. Nothing is known about the state of polarisation of the high-frequency band. The two frequencies in the second row are highly polarised.

The Raman spectrum of deuteronitric acid has been described by Banerji and Mishra, and by Redlich and Nielsen (*locc. cit.*).

The frequencies in the first row of the list given above have been assigned to their vibrations by Chédin, by Mathieu and Massignon, and by Redlich and Nielsen (*locc. cit.*). All three assignments are in large measure correct, but none is entirely complete and correct.

It is agreed that 610 and 680 cm.$^{-1}$ are the two expected ONO-bending frequencies. The former is shown by its depolarisation, and considerable downward shift in deuteronitric acid, to be associated mainly with the bending of $O\widehat{N}(OH)$ angles. The latter is equally shown by its polarisation, and lack of substantial shift in deuteronitric acid, to be essentially the symmetric bending frequency of the NO_2 group. The fact that this frequency is the higher suggests that the mesomerism, more fully developed in the NO_2 group than in the ON(OH) groups, tends to stiffen the $O\widehat{N}O$ angle relatively to the $O\widehat{N}(OH)$ angles.

It is equally agreed that 925, 1300, and 1675 cm.$^{-1}$ are the three expected ON-stretching frequencies. On account of its value, and the high intensity and polarisation with which it appears, 1300 cm.$^{-1}$ is assumed to be essentially the symmetric stretching frequency of the NO_2 group. The other considerably polarised frequency, 925 cm.$^{-1}$, may be assumed to be associated largely with stretching of the N(OH) bond. These frequencies seem reasonably related, having regard to the mesomeric orders of the bonds. The frequency 1675 cm.$^{-1}$ is shown by its depolarisation to represent a highly dissymmetric mode of motion, evidently antisymmetric stretching in the NO_2 group.

The band at 3400 cm.$^{-1}$ certainly arises from OH-stretching motion. The origin of the line at 1535 cm.$^{-1}$ has never been made clear: this will be discussed below.

Further frequencies have been reported which are less well confirmed than these. A weak frequency, 480 cm.$^{-1}$, has been reported by Redlich and Nielsen, who have attributed it, very reasonably, to out-of-plane hydrogen motion. A frequency near 1110 cm.$^{-1}$ has been reported more than once; nevertheless its existence seems doubtful.

Two further fundamental vibrations of the nitric acid molecule exist, whose frequencies have not yet been identified correctly or with certainty in the Raman spectrum. They are the out-of-plane vibration of the NO_2 group, and the hydrogen-bending vibration involving deformation of the HON angle. Further reference to these vibrations is made below.

(1.2) *Assignment of the Raman Frequency* 1535 *cm.*$^{-1}$.—This line was first assigned by Chédin as the combination tone, $610 + 925 = 1535$ cm.$^{-1}$, simply on the ground that the frequencies agree. However, as Mathieu and Massignon observed, the line is too highly polarised to admit of this interpretation. (A binary combination tone derived from a polarised and a depolarised fundamental frequency should be depolarised.) Furthermore, as Redlich and Nielsen pointed out, the interpretation requires an isotope shift in deuteronitric acid of 40 cm.$^{-1}$, whereas in fact the line is not shifted.

Redlich and Nielsen assigned the line to the fundamental out-of-plane frequency of the NO_2 group. But this seems impossible on the following grounds. First, for the reason explained below, a Raman line representing this fundamental vibration should be *extremely* weak—much weaker, almost certainly, than the line at 1535 cm.$^{-1}$ (cf. Fig. 2). Secondly, such a Raman line should be fully depolarised, whereas the actual line is considerably polarised. Thirdly, the corresponding fundamental frequency of the nitrate ion, with its slightly smaller mass, and considerably more fully developed mesomerism, is only 830 cm.$^{-1}$, as is known from the infra-red study of nitrates. The analogous frequency of the nitric acid molecule could hardly be greater than this, and, essentially on account of the diminished mesomerism, would be expected to be somewhat smaller.

The frequency 1535 cm.$^{-1}$ is now assigned as the first overtone of the out-of-plane vibration of the NO_3 group. The corresponding fundamental frequency, 770 cm.$^{-1}$ according to this interpretation, is not likely to be visible in the Raman spectrum, even though it is not forbidden by symmetry; for in the nitrate ion, the corresponding fundamental frequency is forbidden by symmetry in the Raman effect, and all that makes this type of vibration in the nitric acid molecule allowed in principle is the possibility of coupling between this motion and the restricted rotation of the hydrogen atom. However, any such coupling must be extremely weak. It is therefore intrinsically likely that the out-of-plane vibration of the NO_3 group of the nitric acid molecule will be represented in the Raman spectrum considerably more strongly by its first overtone than by its " practically forbidden " fundamental frequency; for the first overtone, though limited as to amplitude by the anharmonicity of the vibration, is of the right symmetry for a strong appearance in the Raman spectrum.

The same spectral properties of this line at 1535 cm.$^{-1}$, which disprove the former interpretations, confirm this one. For first, the vibrational wave-function being totally symmetrical, not only with respect to the whole molecule, but also with respect to the NO_3 group, the Raman line should be considerably polarised. Secondly, since there can be no appreciable coupling between the out-of-plane NO_3 motion and out-of-plane hydrogen motion, neither the fundamental frequency nor its first overtone should show any isotope shift when the mass of the hydrogen atom is changed.

(1.3) *Assignment of the Infra-red Frequency* 780 *cm.*$^{-1}$.—The infra-red spectrum of nitric acid has been observed over the range 6—15 μ. by Freymann and Freymann (*Compt. rend.*, 1946, **222**, 1339). They report bands corresponding to all the main Raman lines falling within this spectral range, together with one further band in the region 770—790 cm.$^{-1}$. Very tentatively they suggested that this might be the fundamental band of the out-of-plane NO_3 vibration. The arguments of the preceding section show that these authors' suggestion is almost certainly correct.

It can be predicted that the corresponding infra-red frequency of deuteronitric acid will also be found at 780 cm.$^{-1}$.

(1.4) *The Hydrogen-bending Vibration.*—For the purpose of assigning a frequency to this vibration, Redlich and Nielsen assumed the Raman line at 1675 cm.$^{-1}$ to be double; but experimentally they could find no sign of doubling, and that is also the experience of the present authors (cf. Fig. 2).

As the hydrogen-bending frequency of deuteronitric acid, Redlich and Nielsen offer a frequency of about 1340 cm.$^{-1}$, represented by a bulge on the high-frequency flank of the contour of the strong line near 1300 cm.$^{-1}$. It has been found in the course of the present experiments that the contour of the line at 1300 cm.$^{-1}$ of ordinary nitric acid likewise contains a bulge on the high-frequency side (cf. Fig. 2). The frequency responsible for this bulge is estimated as about 1360 cm.$^{-1}$. It is obviously possible that these frequencies, neither of which can be determined accurately, have a common origin in the first overtone of the $\widehat{ONO}$-bending vibration, whose fundamental frequency is 680 cm.$^{-1}$ in ordinary nitric acid, and is only slightly reduced in deuteronitric acid.

Owing to the largely ionic character of the OH-bond of nitric acid, the hydrogen-bending frequency is expected to be extremely weak in the Raman effect, probably unobservably weak under the conditions of the present experiments, just as the frequency due to the restricted rotation of the hydrogen atom is unobservably weak. Certainly all the frequencies which have been observed in the course of the present experiments can be understood without appealing to either of these vibrations, whose frequencies will be sought in the infra-red spectrum, where they should appear strongly.

(1.5) *The Breadth of the Raman Lines.*—The great breadth of the hydrogen-stretching Raman band near 3400 cm.$^{-1}$ undoubtedly arises from the intermolecular hydrogen-bonding in liquid nitric acid, as Chédin and Fénéant have pointed out already (*loc. cit.*). Hydrogen-bonding should also cause the hydrogen-bending frequency, and the restricted-rotational hydrogen frequency, to be represented by diffuse bands in the Raman spectrum of liquid nitric acid; their small total intensity being thus smeared out, this may be another reason why we have not observed them.

Most of the other Raman frequencies of liquid nitric acid, though not as broad as the high-frequency band, are still remarkably broad. Thus, in some of our photographs, the total contour of the line having its intensity maximum near 1300 cm.$^{-1}$ extends over about 250 cm.$^{-1}$. Obviously this strong line could obscure a very weak one at distances up to 100 cm.$^{-1}$ away from its intensity maximum, unless the weak line were particularly sharp. This limitation which

the breadth of the strong lines imposes on the observation of neighbouring weak ones is of importance for the understanding of the self-ionisation spectrum of nitric acid. No doubt the cause of the unusual breadth of the Raman lines of nitric acid is, once again, intermolecular hydrogen-bonding.

(2) *Raman Spectra of Mixtures of Nitric Acid and Water.*

(2.1) *General Effects of Added Water on the Nitric Acid Spectrum.*—One of the first effects on the Raman spectrum of nitric acid of the progressive addition of water to the nitric acid is the suppression of the self-ionisation spectrum, which is to be considered in Section 4. Another early effect of added water is to change the forms of hydrogen-bonding doubtless through the production of a hydrogen-bonded hydrate of nitric acid, and thus to produce modifications in the high-frequency band of nitric acid, as has been shown in detail by Chédin and Fénéant (*loc. cit.*). Further amounts of water produce nitrate ion; and we shall be concerned in Sections 3 and 4 with the appearance of the Raman spectrum of the nitrate ion in the presence of a large excess of molecular nitric acid.

(2.2) *The Raman Frequencies of the Nitrate Ion.*—Only the three planar vibrations of the nitrate ion, one totally symmetrical and two doubly degenerate, are allowed to record their fundamental frequencies in the Raman spectrum. The single out-of-plane vibration is forbidden as a fundamental, though its first overtone is allowed.

The literature contains a number of records of the Raman spectra of mixtures of nitric acid and water. Difficulties attended the first attempts to identify the nitrate ion frequencies, although it was agreed by Rao, Kinsey, and Woodward that 1050 cm.$^{-1}$ was one of them. The other allowed fundamental frequencies were found, first in solutions of nitrates by Ramaswarmy and then in aqueous nitric acid by Brunetti and Ollando; in cm.$^{-1}$ they are as follows:

720 (w) 1050 (s) 1360 (w)

(Carelli, Prungsheim, and Rosen, *Z. Physik*, 1928, **51**, 511; Ganesan and Venkateswaran, *Indian J. Physics*, 1929, **4**, 196; Schaefer, Matossi, and Aderhold, *Physikal. Z.*, 1929, **30**, 581; *Z. Physik*, 1930, **65**, 301; Rao, *loc. cit.*; Kinsey, *loc. cit.*; Woodward, *loc. cit.*; Ramaswarmy, *Indian J. Physics*, 1930, **5**, 193; Brunetti and Ollando, *Atti Accad. Lincei*, 1931, **13**, 52; Médard and Petitpas, *Compt. rend.*, 1933, **197**, 1221; Venkateswaran, *Phil. Mag.*, 1933, **15**, 263; *Proc. Indian Acad. Sci.*, 1936, *A*, **4**, 174; Chédin, *Ann. Chim.*, 1937, **8**, 284; Kujumzelis, *Z. Physik*, 1938, **109**, 586; Redlich and Bigeleisen, *J. Amer. Chem. Soc.*, 1943, **65**, 1883).

Venkateswaran found the strong line at 1050 cm.$^{-1}$ to be highly polarised, a result which proves that it belongs to the totally symmetrical vibration of the ion. He found the two weak lines to be depolarised, and this shows that they belong to the degenerate bending, and degenerate stretching, vibrations of the nitrate ion.

The Raman line at 1050 cm.$^{-1}$, because it is strong and well separated from any Raman frequency of molecular nitric acid, is a good index of nitrate ion concentration. On the contrary, not only are the other two active fundamentals, 720 and 1360 cm.$^{-1}$, quite weak, but also the upper one is broad, and each lies fairly close to an important frequency of the nitric acid molecule. These nitric acid frequencies, 680 and 1300 cm.$^{-1}$, are strong and broad; and therefore each overlaps the nitrate ion frequency in its neighbourhood.

Reference may be made to some additional nitrate ion frequencies, which have been observed by the use of crystalline nitrates. The out-of-plane fundamental of the nitrate ion, though forbidden in the Raman effect, is allowed in the infra-red spectrum; and it has been observed as a band at 831 cm.$^{-1}$ in the infra-red spectrum of crystalline sodium nitrate (Schaefer and Schubert, *Ann. Physik*, 1918, **55**, 577). In the Raman spectrum of the same substance, there have been observed the three planar fundamental frequencies of the nitrate ion, some quite low frequencies belonging to lattice vibrations, and one additional, very weak frequency, 1665 cm.$^{-1}$ (Krishnamurti, *Indian J. Physics*, 1930, **5**, 1; Schaefer, Matossi, and Aderhold, *Z. Physik*, 1930, **65**, 289). There can be little doubt that this last frequency is the allowed first overtone of the out-of-plane vibration of the nitrate ion.

(3) *Raman Spectra of Mixtures of Nitric Acid and Dinitrogen Pentoxide.*

(3.1) *Ionisation of Dinitrogen Pentoxide.*—The Raman spectra of solutions of dinitrogen pentoxide in nitric acid have been described by Briner and Susz (*Helv. Chim. Acta*, 1935, **18**, 378), and by Chédin (*Compt. rend.*, 1935, **200**, 1397; *Ann. Chim.*, 1937, **8**, 243). It is agreed, and is confirmed in the present work, that the spectrum contains all the lines of molecular nitric acid,

and in addition two lines, having the frequencies 1050 and 1400 cm.$^{-1}$, and intensities which are approximately proportional to the concentration of dinitrogen pentoxide. Chédin observed, and it is here confirmed, that the spectrum does not contain any of the Raman frequencies of molecular dinitrogen pentoxide, several of which, *viz.* (in cm.$^{-1}$),

860 (w) 1244 (ms) 1335 (s, sharp)

are diagnostically serviceable, as was proved by observations on the Raman spectra of dinitrogen pentoxide in neutral solvents (Chédin, *Compt. rend.*, 1935, **201**, 552; Chédin and Pradier, *ibid.*, 1936, **203**, 772; cf. Chédin, *Ann. Chim.*, 1937, **8**, 243).

The Raman line at 1400 cm.$^{-1}$ has been identified as the totally symmetrical fundamental of the nitronium ion (Part I, *J.*, 1950, 2576). We know that the strongest Raman frequency of the nitrate ion lies at 1050 cm.$^{-1}$ (Section 2.2), and it will be shown below (Section 3.2) that the line found at this frequency along with the line at 1400 cm.$^{-1}$, in the spectra of solutions of dinitrogen pentoxide in nitric acid, in fact belongs to the nitrate ion. The formation of the two ions may be represented thus:

$$N_2O_5 = NO_2^+ + NO_3^-$$

The complete absence from the relevant spectra of lines due to molecular dinitrogen pentoxide shows that this electrolytic dissociation is quantitative.

(3.2) *Identification of the Nitrate Ion.*—It will now be shown that all the appearances that are to be expected from the presence of the nitrate ion are found in the Raman spectrum of a solution of dinitrogen pentoxide in nitric acid.

For this purpose it is convenient to compare the Raman spectrum of a solution of dinitrogen pentoxide in nitric acid with that of a solution of ammonium nitrate in nitric acid. Table I records some frequency displacements measured in Raman spectra of solutions of these types, as well as in the Raman spectrum of anhydrous nitric acid, the measurements relating to Stokes lines excited by nitrite-filtered Hg 4358 A. The assignment of the lines is indicated in Table I, partly in anticipation of the following discussion.

TABLE I.

Raman frequencies of (i) *anhydrous nitric Acid*, (ii) *a solution*, 6% *by weight, of dinitrogen pentoxide in nitric acid, and* (iii) *a solution*, 15% *by weight, of ammonium nitrate in nitric acid.*

(Frequency separations in cm.$^{-1}$ from Hg 4358 A.)

Assignments to HNO_3.	(i) HNO_3.		(ii) N_2O_5 in HNO_3.		(iii) NH_4NO_3 in HNO_3.		Assignments to ions.
Fundamental	609	ms	609	ms	620	ms	—
Fundamental	677	ms	677	ms	680	ms	—
	—	—	(720) *	vw	720	w	NO_3^-
Fundamental	925	s	929	s	929	s	—
	1049	w	1052	m	1048	s	NO_3^-
Funadmental	1296	vs	1298	vs	1303	vs	—
Overtone †	(1360) *	vw	(1360) *	vw	—	—	(NO_3^-) †
	1392	w	1396	m	—	—	NO_2^+
Overtone	1533	w	1540	w	1540	w	—
Fundamental	1670	m	1677	m	1672	m	—

* Roughly estimated, unresolved frequencies are given in parentheses.

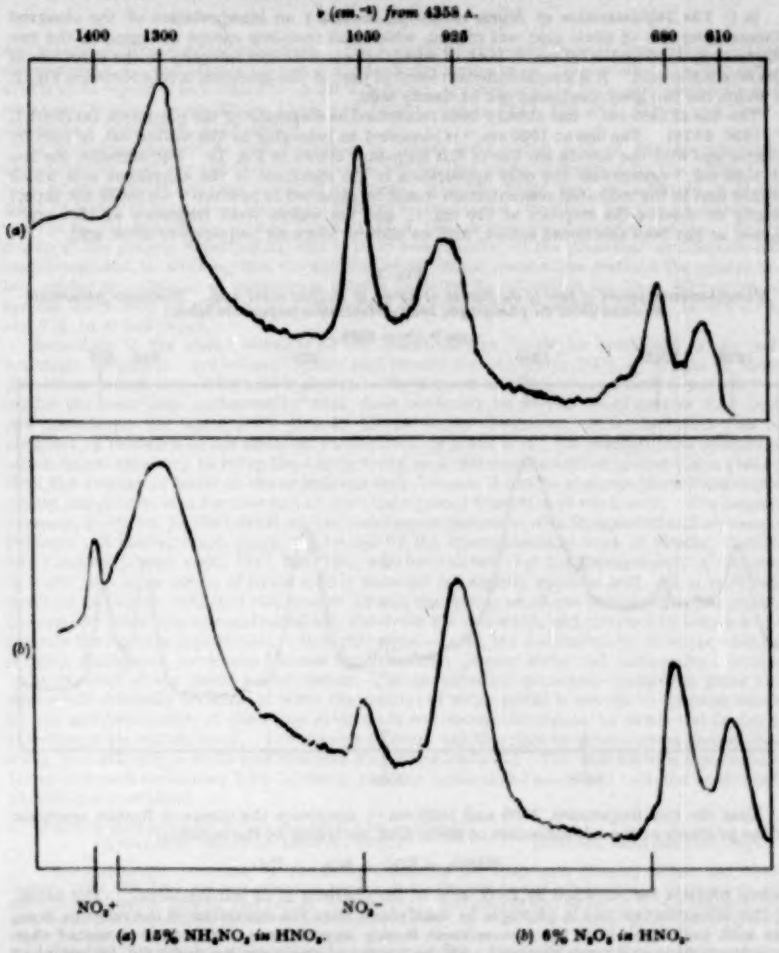
† Part of the intensity of frequency 1360 cm.$^{-1}$ will be due to nitrate ion, and part to the overtone in the nitric acid spectrum.

It is convenient to consider first the spectrum of the solution of ammonium nitrate, a microphotometer record of part of which is shown in Fig. 1a. In this spectrum we see, in addition to nitric acid lines, two of the three Raman fundamentals of the nitrate ion. The totally symmetrical frequency, 1050 cm.$^{-1}$, is strongly developed. The bending frequency, 720 cm.$^{-1}$, is apparent as a just-resolved step-out from the contour of the nitric acid frequency 680 cm.$^{-1}$. The non-totally symmetrical stretching frequency of the nitrate ion, 1360 cm.$^{-1}$, is in any case useless for diagnostic purposes in the presence of nitric acid, because it is overlapped by a nitric acid overtone frequency; and in this particular solution both these frequencies are overlaid by a diffuse band due to the degenerate bending frequencies of the ammonium ion.

Let us now compare these results with those obtained for the solution of dinitrogen pentoxide, a microphotometric record of part of the spectrum of which is reproduced in Fig. 1b. Here we find nitric acid lines, and the nitronium ion line at 1400 cm.$^{-1}$, together with certain appearances

FIG. 1.

Microphotometer records of parts of the Raman spectra, excited by Hg 4358 A., *filtered through nitrite, of* (a) *a solution, 15% by weight, of ammonium nitrate in anhydrous nitric acid, and* (b) *a solution, 6% by weight, of dinitrogen pentoxide in anhydrous nitric acid.*



clearly due to the nitrate ion. The breathing frequency, 1050 cm.$^{-1}$, is prominent, though weaker than before, because of the smaller concentration of nitrate ion. For the same reason, the bending frequency, 720 cm.$^{-1}$, though easily visible, is now weaker, appearing only as an unresolved step-out from the contour of the nitric acid line at 680 cm.$^{-1}$. The third nitrate ion fundamental, 1360 cm.$^{-1}$, in combination with the nitric acid overtone estimated to have about the same frequency, may be considered jointly responsible for the bulge which can be seen on the contour of the nitric acid line at 1300 cm.$^{-1}$, just above the extruding nitronium ion line at

1400 cm.$^{-1}$. Thus all the appearances which the nitrate ion would be expected to produce are found in this spectrum.

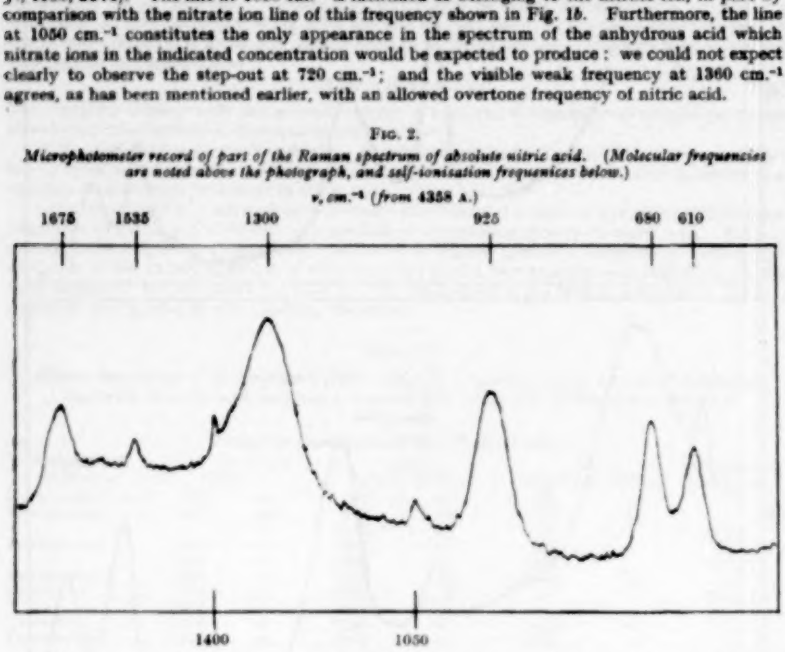
(4) *Raman Spectrum of the Self-ionisation of Nitric Acid.*

(4.1) *The Self-ionisation of Nitric Acid.*—In Section 1 an interpretation of the observed Raman spectrum of nitric acid was offered, which was complete except in regard to the two frequencies, 1400 and 1050 cm.$^{-1}$, both of which appear with low intensity in the spectrum of absolute nitric acid. A microphotometer record of part of this spectrum is reproduced in Fig. 2, in which the two lines mentioned can be clearly seen.

The line at 1400 cm.$^{-1}$ has already been recognised as diagnostic of the nitronium ion (Part I, *J.*, 1950, 2576). The line at 1050 cm.$^{-1}$ is identified as belonging to the nitrate ion, in part by comparison with the nitrate ion line of this frequency shown in Fig. 1*b*. Furthermore, the line at 1050 cm.$^{-1}$ constitutes the only appearance in the spectrum of the anhydrous acid which nitrate ions in the indicated concentration would be expected to produce: we could not expect clearly to observe the step-out at 720 cm.$^{-1}$; and the visible weak frequency at 1360 cm.$^{-1}$ agrees, as has been mentioned earlier, with an allowed overtone frequency of nitric acid.

FIG. 2.

Microphotometer record of part of the Raman spectrum of absolute nitric acid. (Molecular frequencies are noted above the photograph, and self-ionisation frequencies below.)



Thus the two frequencies, 1400 and 1050 cm.$^{-1}$, constitute the observed Raman spectrum of the products of the self-ionisation of nitric acid, according to the equation

$$2HNO_3 = NO_2^+ + NO_3^- + H_2O$$

(which neglects the solvation by nitric acid of the products of its self-ionisation). The extent of this self-ionisation can in principle be determined from the intensities of the relevant lines, but with such weak lines the measurement is only approximate. It is thus estimated that anhydrous nitric acid contains about 1·0% by weight of nitronium ion and 1·5% by weight of nitrate ion, either value being subject to a possible error of 20%. Assuming the above equation to be accurate, and allowing for the water involved, these figures mean that about 3% of anhydrous nitric acid is self-dissociated.

These values may be compared with Gillespie, Hughes, and Ingold's estimate (*J.*, 1950, 2552), based on the rounding of the freezing-point maximum of the system N_2O_5–H_2O at the composition HNO_3, of the total concentration of all self-dissociation products in anhydrous nitric acid. For this total they obtain the value 0·82 molal, which corresponds, if the above

equation is accurate, to nitronium ion, nitrate ion, and water, each in 0·27 molal concentration. Spectroscopically, we find 0·22 molal nitronium ion, and 0·24 molal nitrate ion.

These spectroscopic determinations establish that the above-written ionic self-dehydration is the principal mode of self-dissociation of nitric acid. The alternative is auto-protolysis,

$$2HNO_3 = H_2NO_3^+ + NO_3^-$$

and this reaction may indeed take place. But it cannot be the chief form of dissociation, because the nitronium ion and nitrate ion are in approximate equivalence. Essentially, absolute nitric acid is to be regarded as a dilute (~ molal/4) solution, in nitric acid, of dinitrogen pentoxide and water (cf. Norman Jones, Thorn, Lyne, and Taylor, *Nature*, 1947, **159**, 163; Jones and Thorn, *Canadian J. Res.*, 1949, *B*, **27**, 580).*

(4.2) *Suppression of the Self-ionisation of Nitric Acid.*—One part of the spectroscopic demonstration that the self-ionisation process represented above is reversed by the addition of each of its products has been supplied by Chédin, who has found that the addition of about 1·5% of water to anhydrous nitric acid suffices to render the nitronium ion line unobservably weak in the Raman spectrum (*Ann. Chim.*, 1937, **8**, 243; and personal communication). In the course of the present experiments, this type of confirmation of the presumed equilibrium has been completed, by showing that the addition of nitronium perchlorate destroys the nitrate ion line, whilst the addition of ammonium nitrate destroys the nitronium ion line. The types of spectra which may be obtained by these means are sufficiently illustrated by Fig. 1*a* of Part I, and Fig. 1*a* of this paper.

According to the above estimate of ion concentrations, based on intensities in the self-ionisation spectrum, "anhydrous" nitric acid should contain about 0·4% by weight of water (doubtless present as a nitric acid hydrate). The amount of added water which is necessary to render the ionic lines unobservably weak must obviously be several times greater than this, and accordingly the figure 1·5% give by Chédin seems consistent. A similar check can be obtained by reference to the electrical conductivity of nitric acid; for evidently the amount of added water necessary to bring the conductivity to a minimum must be several times greater than the amount of water in the anhydrous acid, because it has to suppress the self-ionisation almost completely, and has also just to start the aqueous ionisation of nitric acid. The amount necessary is 3% (cf. *J.*, 1950, 2422), and this also seems consistent with the spectral and cryoscopic evidence. A similar rough check is provided by the thermochemical work of Chédin, Leclerc, and Vandoni (*Compt. rend.*, 1947, **225**, 734), who have shown that the exothermicity of addition of water to a large excess of nitric acid is maximal for slightly aqueous acid. It is relatively small for anhydrous acid (and still smaller for acid containing an excess of dinitrogen pentoxide), because the water has to endothermically desolvate the nitronium and nitrate ions before it can hydrate the dinitrogen pentoxide. In highly aqueous acid, the exothermicity of water addition is again diminished, obviously because the previously present water will reduce the solvation by nitric acid of the newly added water. The endothermic maximum separating those two effects will evidently be attained when the amount of water added is enough to suppress nearly all the self-dissociation of the nitric acid but is not enough to reduce by much the degree of solvation of the added water. The amount of water will therefore be several times greater than 0·4%, but still only a small mol.-fraction (*i.e.*, a few units %). The endothermic maximum is found with acid containing 2·5% of water, and this again seems consistent with the other kinds of evidence mentioned.

William Ramsay and Ralph Forster Laboratories,
University College, London, W.C.1. [*Received, December* 17*th*, 1949.]

* Since dinitrogen pentoxide is completely ionised in the solid state (Ingold, Millen, and Poole, *Nature*, 1946, **158**, 480; see also preceding paper), and is likewise completely ionised in dilute solution in nitric acid (Gillespie, Hughes, and Ingold, *J.*, 1950, 2552; Section 3 of this paper), it is just as true to say that a solution prepared by dissolving dinitrogen pentoxide in nitric acid *contains* dinitrogen pentoxide, as that a solution of sodium chloride in water contains sodium chloride: for in either case, when the solid dissolves, the ions fall apart without covalency change. Generally, any solution, which contains nitronium and nitrate ions, contains dinitrogen pentoxide, which (as ordinarily seen and preserved) is an ionic substance. Thus Briner and Susz were correct when they ascribed to dinitrogen pentoxide the Raman frequencies 1400 and 1050 cm.$^{-1}$, observed in the spectrum of nitric oleum, as was Chédin when he similarly assigned the same frequencies, found in the spectrum of anhydrous nitric acid. Berl was likewise correct in assuming the solvation of dinitrogen pentoxide by nitric acid in explanation of the vapour pressures of his solutions. These remarks are made in qualification of Bennett, Brand, and Williams's criticism of what they call "the nitrogen pentoxide hypothesis" (*J.*, 1946, 874).

511. *Vibrational Spectra of Ionic Forms of Oxides and Oxy-acids of Nitrogen. Part VI. Raman-spectral Evidence of the Ionisation of Dinitrogen Tetroxide in Nitric Acid. The Nitrosonium Ion, NO^+, and the Nitrosonium–Nitrogen Dioxide Ion, $N_2O_3^+$.*

By J. D. S. Goulden and D. J. Millen.

The Raman spectra of solutions of dinitrogen tetroxide in nitric acid have been studied. The spectrum of the dinitrogen tetroxide molecule is completely absent. The strongest appearances, apart from solvent lines, are a line at 2240 cm.$^{-1}$, which can only belong to the nitrosonium ion in some form (see below), and one at 1050 cm.$^{-1}$, which is identified as the main nitrate ion frequency. The latter constitutes an intensification of one of the self-ionisation frequencies of the nitric acid solvent; and, consistently, its development is accompanied by a disappearance of the other self-ionisation line, 1400 cm.$^{-1}$, belonging to the nitronium ion. The solute spectrum contains also a somewhat weak frequency 1380 cm.$^{-1}$, which is assumed to be the totally symmetrical fundamental of the nitrogen dioxide molecule, a frequency hitherto observed only as a weak band in the infra-red. It is concluded that the dinitrogen tetroxide molecule, in dilute solution in nitric acid, is almost completely dissociated, partly homolytically, but chiefly heterolytically, as follows:

$$2NO_2 \rightleftharpoons N_2O_4 \rightleftharpoons NO^+ + NO_3^-$$

The frequency of the nitrosonium ion is usually found at about 2300 cm.$^{-1}$, though the value varies a little with the conditions of solvation. The value 2240 cm.$^{-1}$, obtained in nitric acid, is, however, outside the usual range of variation; and it is shown to arise from a modification of the nitrosonium ion by some specific molecular interaction, because, in the spectra of solutions of nitrosonium hydrogen sulphate and nitrosonium perchlorate in nitric acid, the modified and unmodified frequencies can be seen side by side. By examining the effect of various added substances on the intensities of the modified and unmodified frequencies, the modifying agent is identified as the nitrogen dioxide molecule. It is assumed to form a molecular compound, NO^+,NO_2, held together by a partly homopolar, but mainly electrostatic, one-electron bond.

(1) *Raman Spectra of Solutions of Dinitrogen Tetroxide in Nitric Acid.*

(1.1) *Correlation of Chemical, Electrical, and Spectral Properties of the Solutions.*—It has been suggested (Hughes, Ingold, and Reed, *J.*, 1950, 2400), on the basis of a kinetic study of the effect of dinitrogen tetroxide on nitration in certain media, that the substance is ionised by nitric acid to produce nitrosonium and nitrate ions:

$$N_2O_4 \rightleftharpoons NO^+ + NO_3^-$$

Strong evidence that dinitrogen tetroxide is ionised by nitric acid has been provided by electrochemical work which will be published shortly. It has been shown that solutions of dinitrogen tetroxide in nitric acid have electrical conductances of the same order as those found for solutions of equivalent concentration of alkali nitrates. This establishes not only that dinitrogen tetroxide ionises in nitric acid, but also that it cannot be regarded as a weak electrolyte.

It has also been shown that the addition of alkali nitrates to solutions of dinitrogen tetroxide in nitric acid has the specific effect of increasing the vapour pressure of the solute. The effect may be interpreted as a mass-law repression of the suggested ionisation.

The equation written above for the ionisation of dinitrogen tetroxide in nitric acid has also been used to express the presumed self-ionisation of pure liquid dinitrogen tetroxide (Addison and Thompson, *J.*, 1949, S211 and S218).

The present paper provides Raman-spectroscopic evidence which confirms the suggested ionisation of dinitrogen tetroxide in nitric acid solution. The observation of the Raman spectra of these solutions is rendered difficult by absorption which extends throughout the visible part of the spectrum, is particularly intense in the blue, and continues into the ultra-violet. For this reason we have excited Raman spectra by the green line Hg 5461 A. In these spectra the strong yellow lines Hg 5770 A. and Hg 5790 A. obscure Raman frequencies from about 940 cm.$^{-1}$ to 1080 cm.$^{-1}$. By using a technique which reduces the paths of both incident and Raman radiations to a minimum, we have obtained a spectrum of a dilute solution by excitation by Hg 4358 A., which provides information about that part of the spectrum which is obscured in the spectra excited by Hg 5461 A.

(1.2) *Raman Spectra of the Solutions compared with the Spectra of the Components.*—The frequencies in the Raman spectra of a number of solutions of dinitrogen tetroxide in nitric acid are recorded in Table I. The frequencies in the spectra of the materials from which the solutions are derived are included for comparison. The Raman displacements which we find for liquid dinitrogen tetroxide at $-10°$ are consistent with those which were found for the solid by Sutherland (*Proc. Roy. Soc.*, **1933**, *A*, **141**, 342). The Raman spectrum of nitrogen dioxide has not been observed because it absorbs so strongly throughout the visible spectrum. Two of its fundamentals, $\nu_2 = 648$ cm.$^{-1}$ and $\nu_3 = 1621$ cm.$^{-1}$, have been obtained from the infra-red spectrum (Sutherland, *Proc. Roy. Soc.*, **1934**, *A*, **146**, 278). There are two possibilities for the third fundamental: Sutherland (*loc. cit.*, **1934**) and Schaffert (*J. Chem. Physics*, **1933**, **1**, 507) suppose that the weak band at 1373 cm.$^{-1}$ in the infra-red spectrum corresponds to ν_1. Harris, Benedict, and King (*Nature*, **1933**, **131**, 621), in consequence of a study of the ultra-violet absorption spectrum, suggested that ν_1 has the value 1320 cm.$^{-1}$.†

TABLE I.

Raman frequencies (in cm.$^{-1}$) of solutions of dinitrogen tetroxide in pure nitric acid.

(The frequencies in cols. 1 and 2 were excited by Hg 4358 A., and those in cols. 3—7 by Hg 5461 A. As to col. 8, see the text.)

(1). Pure HNO_3.	(2.) 1% N_2O_4 in HNO_3.	(3). 1% N_2O_4 in HNO_3.	(4). 4% N_2O_4 in HNO_3.	(5). 6% N_2O_4 in HNO_3.	(6). 8·7% N_2O_4 in HNO_3.	(7). Liquid N_2O_4.	(8). Fundamentals of NO_2.
609 ms	605 ms	617 ms	602 ms	615 ms	617 ms	265 vs	648
679 ms	675 ms	672 ms	677 ms	690 ms	682 ms	500 m	1320 or 1373
925 s	925 s	937 s	925 s	925 s	930 s	811 s	
1049 w *	1045 mw	—	→	—	—	1325 mw	1621
1295 s	1300 s	1305 s	1295 s	1300 s	1307 s	1382 s	
1392 w *	—	—	—	—	—	1724 ms	
1533 w	—	1555 w	1532 w	—	1546 w		
1670 m	1680 m	1680 m	1675 m	1685 m	1687 m		
—	—	2232 mw	2238 m	2245 ms	2238 s		

* Self-ionisation line.

The spectrum of the solution excited by Hg 4358 A. (column 2) shows that, in addition to the frequencies of the nitric acid molecule, there is also present a frequency of 1045 cm.$^{-1}$. The intense absorption in the blue region shown by the more concentrated solutions has necessitated excitation of Raman spectra by Hg 5461 A., which carries with it the disadvantage that the frequency 1045 cm.$^{-1}$ will be obscured by the strong yellow lines Hg 5770 A. and Hg 5790 A. The spectra given in columns 3—6 contain a frequency of 2240 cm.$^{-1}$, which increases in intensity with increasing concentration of dinitrogen tetroxide. A frequency of 2240 cm.$^{-1}$ excited by Hg 4358 A. would fall in a region of the spectrum which is out of focus when the spectrograph is adjusted to record Stokes lines from about 100 cm.$^{-1}$ to 1700 cm.$^{-1}$, and this is doubtless the reason why this frequency is missing from the spectrum given in column 2.

(1.3) *Spectroscopic Identification of the Ions Present in the Solution.*—The only measured lines of the solutions of dinitrogen tetroxide in nitric acid which cannot be attributed to the nitric acid molecule are those at 1045 cm.$^{-1}$ and 2240 cm.$^{-1}$. The former appears in the spectrum of anhydrous nitric acid, but there it is accompanied by a line at 1392 cm.$^{-1}$. It will be recalled that in Part V the frequencies 1045 cm.$^{-1}$ and 1392 cm.$^{-1}$ were assigned respectively to the nitrate and nitronium ions, which are produced, together with a solvated water molecule, by the self-ionisation:

$$2HNO_3 \rightleftharpoons NO_2^+ + NO_3^- + H_2O$$

In the spectrum of a dilute solution of dinitrogen tetroxide in nitric acid, the recording of a weak line at 1045 cm.$^{-1}$ in the absence of a line at 1400 cm.$^{-1}$ cannot be due to differential absorption, since this would favour the appearance of 1400 cm.$^{-1}$. We may easily account for this result if we assume that dinitrogen tetroxide ionises in nitric acid producing nitrate ions. This will lead to a strengthening of the line at 1045 cm.$^{-1}$, and a reduction in intensity

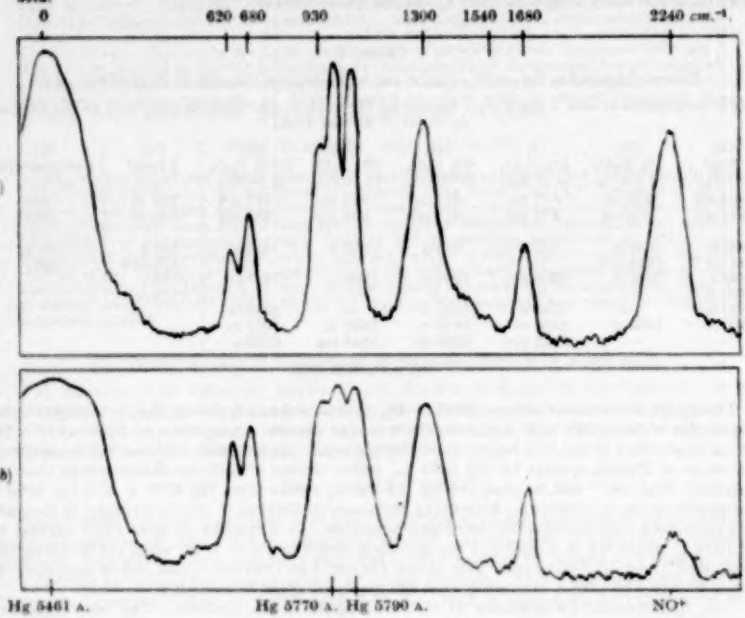
† However, there seems to be an inconsistency somewhere in their analysis, because they find $\nu_2 = 750$ cm.$^{-1}$, whereas it can hardly be doubted that the correct value is the directly observed one, $\nu_2 = 648$ cm.$^{-1}$ (cf. Harris, King, Benedict, and Pearse, *J. Chem. Physics*, **1940**, **8**, 765).

of the nitronium ion frequency of 1400 cm.$^{-1}$, as a consequence of the repression of the self-ionisation of nitric acid. The absence of the remaining two fundamental frequencies of the nitrate ion * is attributed to their low intensity compared with the frequency 1050 cm.$^{-1}$ (cf. Part V).

It is seen from columns 7 and 8 of Table I that the frequency 2240 cm.$^{-1}$ is not a fundamental of the nitrogen dioxide or dinitrogen tetroxide molecule. It cannot be an overtone or combination vibration of either of these molecules, for, as the microphotometer record reproduced in Fig. 1 (*a*) shows, it is too intense to permit this interpretation. We assign the frequency

FIG. 1.

Microphotometer records of the Raman spectra excited by Hg 5461 A., *of* (a) *a solution, 8·7% by weight, of dinitrogen tetroxide in nitric acid, and* (b) *a solution, 0·5% by weight, of dinitrogen tetroxide in nitric acid.*



to a form of the nitrosonium ion. The highest value of the frequency observed for these solutions is lower than any value hitherto reported for the NO^+ ion, but it is known that the fundamental vibration frequency of the ion is sensitive to change of environment. For crystalline nitrosonium perchlorate the value is 2320 cm.$^{-1}$ (Angus and Leckie, *Trans. Faraday Soc.*, 1935, **31**, 958), while for a solution of dinitrogen trioxide in aqueous sulphuric acid a value for the nitrosonium ion frequency as low as 2290 cm.$^{-1}$ was obtained (Part III, *J.*, 1950, 2600). The significance of the particularly low value of the nitrosonium ion frequency in nitric acid solutions is discussed in Section 2.

The assignments made above lead to the conclusion that dinitrogen tetroxide is ionised in nitric acid according to the equation

$$N_2O_4 \rightleftharpoons NO^+ + NO_3^-$$

There is no spectral evidence of the formation of nitronium or nitrite ions.

* One of them, 720 cm.$^{-1}$, is doubtfully visible in Fig. 1*a*. The other, 1360 cm.$^{-1}$, is overlaid by a stronger frequency of different origin (Section 1·4).

(1.4) *Spectroscopic Evidence concerning the Non-ionised Solute Species.*—The frequencies which appear as separate lines in the spectra of these solutions have now been assigned. It is seen from the microphotometer record of the 8·7% solution (Fig. 1) that in addition to these lines there is an unresolved step-out from the strong nitric acid line at 1300 cm.$^{-1}$. It corresponds to the presence of a frequency of about 1380 cm.$^{-1}$. A nitric acid combination tone and a nitrate ion fundamental occur in this region (Part V, *J.*, 1950, 2612), but the appearance in the present spectrum seems too strong to be attributed to either of these. It may be explained by supposing the solution to contain non-ionised nitrogen dioxide, if the assignment of the fundamentals of this molecule by Sutherland and Schaffert is accepted; for that assignment implies that the strongest Raman frequency of the nitrogen dioxide molecule would have a value of about 1373 cm.$^{-1}$. The yellow colour of the solutions is consistent with the presence of non-ionised nitrogen dioxide. The other two fundamental frequencies of the nitrogen dioxide molecule, 648 cm.$^{-1}$ and 1621 cm.$^{-1}$, are not apparent in the microphotometer record reproduced in Fig. 1, but this could hardly be expected since these two frequencies will occur only weakly in the Raman spectrum, and will be masked by the strong nitric acid lines 610 cm.$^{-1}$, 680 cm.$^{-1}$, and 1675 cm.$^{-1}$.

The distinctive characteristics in the spectrum of the dinitrogen tetroxide molecule, which would serve to identify it in the present case, are the strong lines at 810 cm.$^{-1}$ and 1722 cm.$^{-1}$, and especially the very strong and sharp line at 265 cm.$^{-1}$. None of these frequencies is evident in the microphotometer records of the spectra of solutions of dinitrogen tetroxide in nitric acid. It may therefore be safely concluded that the concentration of non-ionised dinitrogen tetroxide in these solutions is very small.

(2) *The Influence of Environment on the Nitrosonium Ion Frequency.*

(2.1) *Raman Spectra of Solutions of Nitrosonium Perchlorate and of Nitrosonium Hydrogen Sulphate in Nitric Acid.*—The frequencies in the Raman spectra of 4% solutions of dinitrogen tetroxide, nitrosonium hydrogen sulphate, and nitrosonium perchlorate, and in the spectrum of a 10% solution of nitrosonium hydrogen sulphate are recorded in Table II. The frequencies were measured as Stokes lines excited by Hg 5461 A. The frequencies recorded in parentheses have been measured as incompletely resolved lines.

TABLE II.

Raman frequencies (in cm.$^{-1}$) observed in the spectra of nitrosonium salts and dinitrogen tetroxide in nitric acid.

4% N_2O_4 in HNO_3.	4% $(NO)ClO_4$ in HNO_3.	4% $(NO)HSO_4$ in HNO_3.	10% $(NO)HSO_4$ in HNO_3.	4% N_2O_4 in HNO_3.	4% $(NO)ClO_4$ in HNO_3.	4% $(NO)HSO_4$ in HNO_3.	10% $(NO)HSO_4$ in HNO_3.
—	471 w	—	—	—	1400 w	1400 w	1400 w
602 ms	617 ms	614 ms	611 ms	—	1533 s	1545 w	—
677 ms	679 ms	677 ms	676 ms	1675 m	1689 m	1680 m	1675 m
925 s	930 s	929 s	928 s	2238 ms	(2240 w)	(2240 mw)	(2243 mw)
1295 s	1302 s	1300 s	1295 s	—	2305 m	(2290 mw)	2285 m

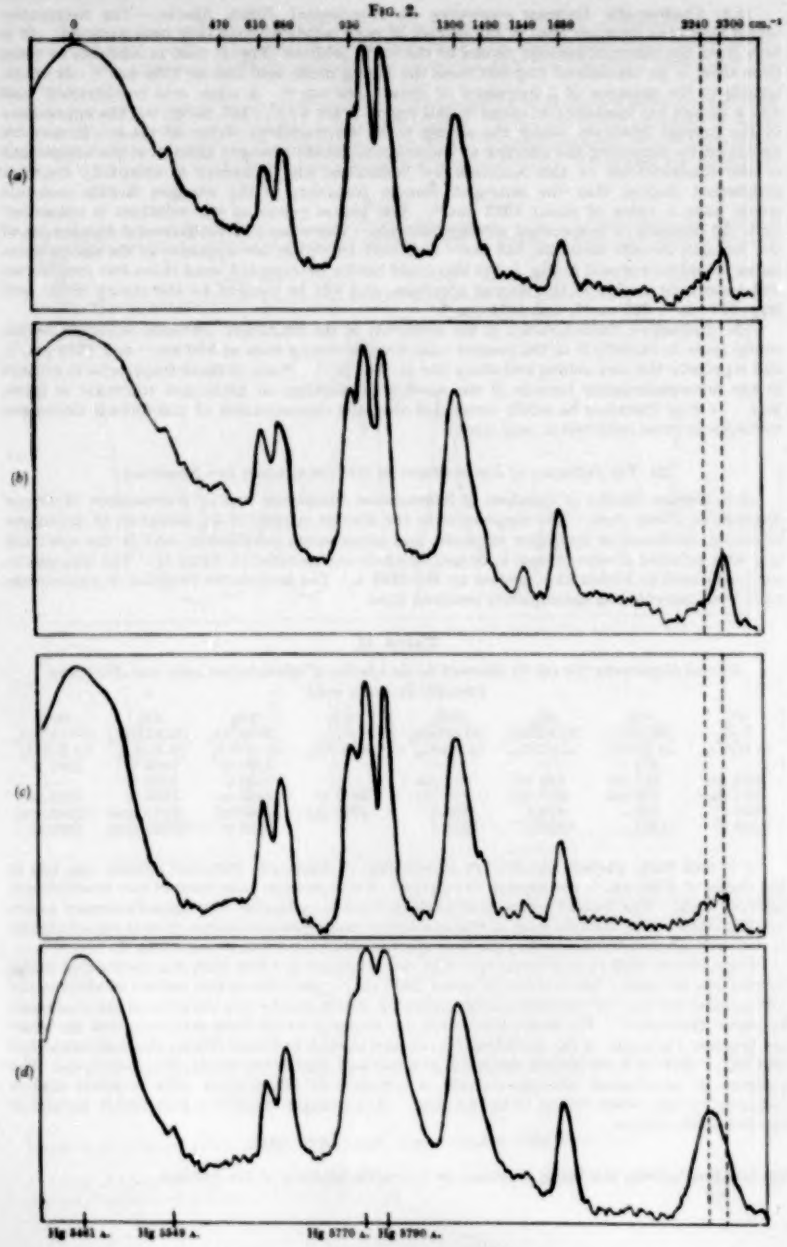
It is seen that, whereas the spectra of solutions of dinitrogen tetroxide contain one line in the region of 2300 cm.$^{-1}$, the spectra of solutions of nitrosonium salts contain two incompletely resolved lines. The weaker component of these has approximately the same frequency as the one line observed in the spectrum of the solution of dinitrogen tetroxide. This is shown clearly in the microphotometer records of the four spectra which are reproduced in Fig. 2.

These results lead to the conclusion that, for solutions in nitric acid, the unmodified nitrosonium ion frequency has a value of about 2300 cm.$^{-1}$, and that under certain conditions the nitrosonium ion may be modified in some manner, which results in a lowering of the frequency to about 2240 cm.$^{-1}$. The molecules which are common to all these solutions, and therefore are possibly the cause of the modification, are the solvent molecule HNO_3, the molecules H_2O and NO_3^-, derived from the self-ionisation of nitric acid, and the molecules NO_2 and N_2O_4. The presence of non-ionised nitrogen dioxide in solutions of nitrosonium salts in nitric acid is indicated by the yellow colour of the solution. The nitrogen dioxide is presumably formed in the balanced reaction,

$$NO^+ + NO_3^- \rightleftharpoons N_2O_4 \rightleftharpoons 2NO_2$$

the involved nitrate ion being provided by the self-ionisation of the solvent.

FIG. 2.


0
470
610
880
930
1300
1400
1540
1650
2240
2300 cm.⁻¹
(a)
(b)
(c)
(d)
Hg 4461 A.
Hg 4849 A.
Hg 5770 A.
Hg 5790 A.

(2.2) *Raman Spectra of Solutions of Dinitrogen Tetroxide in Sulphuric Acid. Effect of the Addition of* (a) *Water*, (b) *Nitric Acid.*—The conditions which favour the appearance of the modified nitrosonium ion frequency have been investigated by a systematic study of the effect of different added substances.

In order to obtain the number of spectra required, it has been necessary to use arcs producing a higher intensity of 5461 A. than that obtained from the low-pressure arcs used for the work so far reported. The reduction in exposure time has been accompanied by some loss in resolving power owing to the increased breadth of the line Hg 5461 A. from the new source.

The results obtained for the addition of water and of nitric acid to a solution of dinitrogen tetroxide in sulphuric acid are given in Tables III and IV, respectively. Only a few of the most characteristic frequencies, which were all measured as Stokes lines excited by Hg 5461 A., are listed.

TABLE III.

The effect on the Raman spectra of the addition of water to a 10% solution of dinitrogen tetroxide in sulphuric acid.

Mols. H_2O / Mols. H_2SO_4	Characteristic frequencies ($cm.^{-1}$). NO_2^+.	H_2SO_4.	HNO_3.	NO^+.	Mols. H_2O / Mols. H_2SO_4	Characteristic frequencies ($cm.^{-1}$). NO_2^+.	H_2SO_4.	HNO_3.	NO^+.
0	1406	905	—	2298	1·07	—	—	—	2288
0·12	1409	906	—	2298	1·51	—	—	1295	2282
0·32	1405	917	—	2299	2·02	—	—	1310	2272
0·53	—	915	—	2288	2·59	—	—	vw	2270
0·67	—	913	—	2289	3·26	—	—	—	2260

TABLE IV.

The effect on the Raman spectra of the addition of nitric acid to a 12% solution of dinitrogen tetroxide in sulphuric acid.

Mols. HNO_3 / Mols. H_2SO_4	Characteristic frequencies ($cm.^{-1}$). NO^+.	NO_2^+.	HNO_3.	Mols. HNO_3 / Mols. H_2SO_4	Characteristic frequencies ($cm.^{-1}$). NO^+.	NO_2^+.	HNO_3.
0	2299	1410	—	1·0	2292	1410	1310
0·24	2292	1411	—	2·0	2290	1407	1309
0·5	2289	1407	1305				

(2.3) *Raman Spectra of Solutions of Dinitrogen Tetroxide in Nitric Acid. Effect of the Addition of* (a) *Sulphuric Acid*, (b) *Water*, (c) *Dinitrogen Pentoxide.*—The significant frequencies in the spectra of these solutions are recorded in Tables V, VI, and VII. All the frequencies were measured as Stokes lines excited by Hg 5461 A.

TABLE V.

Effect on the Raman spectra of the addition of sulphuric acid to a 10·6% solution of dinitrogen tetroxide in nitric acid.

Mols. H_2SO_4/Mols. N_2O_4	0·0	0·019	0·050	0·099	0·497	0·995	1·991	2·982
Mols. HNO_3/Mols. H_2SO_4	∞	633	244	124	24·7	12·35	6·18	4·12
Nitrosonium ion frequency ($cm.^{-1}$)	2243	2248	2246	2250	2260	2290	2297	2296

TABLE VI.

Effect on the Raman spectra of the addition of water to a 11·6% solution of dinitrogen tetroxide in nitric acid.

Mols. H_2O/Mols. N_2O_4	0	0·5	1·0	2·0	5·0	10·0	22·1
Mols. H_2O/Mols. HNO_3	0	0·05	0·09	0·18	0·45	0·91	2·00
Nitrosonium ion frequency ($cm.^{-1}$)	2242	2237	2240	2238	2240	2237	vw

EXPLANATION OF FIG. 2.

Microphotometer records of Raman spectra, excited by Hg 5461 A., of (a) *a solution, 10% by weight, of nitrosonium hydrogen sulphate in nitric acid*, (b) *a solution, 4% by weight, of nitrosonium perchlorate in nitric acid*, (c) *a solution, 4% by weight, of nitrosonium hydrogen sulphate in nitric acid, and* (d) *a solution, 6% by weight, of dinitrogen tetroxide in nitric acid.*

TABLE VII.

Effect on the Raman spectra of the addition of dinitrogen pentoxide to a 10% solution of dinitrogen tetroxide in nitric acid.

Mols. N_2O_5/Mols. N_2O_4	0	0·090	0·183	0·452	0·921	1·424
Mols. HNO_3/Mols. N_2O_4	∞	142	69·7	27·8	13·6	8·0
Nitrosonium ion frequency ($cm.^{-1}$)	2240	2242	2237	2235	2238	2233

(2.4) *Cause of the Variation of the Nitrosonium Ion Frequency. The Ion* $N_2O_5^+$.—For water–sulphuric acid solvents the nitrosonium ion frequency varies continuously from about 2340 $cm.^{-1}$, for a solution of the hydrogen sulphate in anhydrous acid (Angus and Leckie, *Proc. Roy. Soc.*, 1935, *A*, **149**, 327), to about 2260 $cm.^{-1}$ for solutions in a largely aqueous medium. The large variation of frequency with change of solvating power of the medium is possibly due to a high polarisability of the triple bond of the nitrosonium ion.

For solutions in nitric acid a different situation arises. Two distinct nitrosonium ion frequencies appear, the lower of which is presumably caused by some specific molecular intervention. It is established by the data in Tables IV, V, VI, and VII that neither nitric acid nor water molecules are concerned in this effect. The presence of nitric acid molecules in the solution does not necessarily result in the appearance of the lower nitrosonium ion frequency, and for solutions in nitric acid neither the addition of water nor its removal by the addition of dinitrogen pentoxide leads to any appreciable change in the nitrosonium ion frequency. The dinitrogen tetroxide molecule may also be excluded since it was shown in Section 1.4 that its concentration in solutions in nitric acid is very small. Evidence that the nitrate ion is not responsible for the modification can also be provided. In an 8·7% solution of dinitrogen tetroxide in nitric acid, nitrosonium and nitrate ions exist in approximately equimolecular proportions, and, as the microphotometer record of the spectrum (Fig. 1) shows, the nitrosonium ion exists in the modified form. But in the spectrum of a 0·31 molal solution of nitrosonium perchlorate, as the microphotometer record of this spectrum (Fig. 2*b*) shows, the unmodified nitrosonium ion frequency appears strongly and the modified one only weakly, although the nitrate ion concentration, provided here by the self-ionisation of the solvent, is about 0·27 molal (cf. Part V). The formation of stable ion-pairs $(NO^+)(NO_3^-)$ is also rendered improbable by the high electrical conductance of solutions of dinitrogen tetroxide in nitric acid.

The spectroscopic results are consistent with the idea that the modification of the nitrosonium ion arises through association with nitrogen dioxide. The spectra of solutions of nitrosonium salts in nitric acid are readily interpreted on this basis. The amount of nitrogen dioxide produced in these solutions is controlled by the equilibrium:

$$NO^+ + NO_3^- \rightleftharpoons 2NO_2$$

The concentration of nitrate ion depends upon the degree of self-ionisation of nitric acid, and also on the equilibria:

$$HNO_3 + ClO_4^- \rightleftharpoons HClO_4 + NO_3^-$$
$$HNO_3 + HSO_4^- \rightleftharpoons H_2SO_4 + NO_3^-$$

The second of these equilibria will be more important for providing nitrate ions (because sulphuric acid is much less strong than perchloric acid), and therefore the concentration of nitrogen dioxide will be greater in the solution of nitrosonium hydrogen sulphate than in that of the perchlorate. Correspondingly, as the microphotometer records in Fig. 2 show, the intensity of the modified frequency relative to the unmodified frequency is higher in the spectrum of the hydrogen sulphate than in that of the perchlorate.

The frequency of the nitrosonium ion in the spectra of solutions of dinitrogen tetroxide in nitric acid is unaffected by the addition of dinitrogen pentoxide or water (Tables VI and VII). Neither of these substances removes non-ionised nitrogen dioxide, and, consistently, all these spectra contain the modified nitrosonium ion frequency. But the addition of increasing quantities of sulphuric acid, which will remove non-ionised nitrogen dioxide by the reaction

$$3H_2SO_4 + 2NO_2 \rightleftharpoons NO^+ + NO_2^+ + H_3O^+ + 3HSO_4^-$$

leads to a sharp rise in the nitrosonium frequency, until it reaches the unmodified value for solutions in nitric acid (Table V). Thus the spectral evidence points fairly definitely to the existence of a molecular compound between the ion NO^+ and the radical NO_2.

It is possible that the compound arises through the formation of a single-electron bond between the ion and the radical, the resonance structures of the compound being

(I.) $\hat{N}O_2\hat{N}O$ and $\hat{N}O_2\hat{N}O$ (II.)

The observed frequency of 2240 cm.$^{-1}$ for the compound is much closer to the frequency of the NO^+ ion (2300 cm.$^{-1}$) than to that of the nitric oxide molecule (1880 cm.$^{-1}$). This is taken to indicate the wave-function for structure (I) makes the greater contribution to the real wave-function of the molecule. It is to be expected that structure (I) will be more important than structure (II), since the NO_2 molecule belongs to a lower state of oxidation than the ion NO_2^+, and the NO^+ ion belongs to a higher state of oxidation than the NO molecule. Thus (I) would have a smaller tendency to pass by a redox electron-transfer into (II) than (II) would have to pass into (I). For these reasons, we regard the ion $N_2O_3^+$ essentially as a modified nitrosonium ion, and name it, accordingly, the nitrosonium–nitrogen dioxide ion.

(3) *Experimental Methods.*

The main methods of obtaining and evaluating spectra were similar to those mentioned in Part I, but certain modifications, which were necessitated by the strong colour of the materials, are described here. Spectra were obtained by using an F/4 Hilger E 5 spectrograph, having a mean dispersion of approximately 70 A. per mm. for spectra excited by Hg 4358 A., and approximately 150 A. per mm. for spectra excited by Hg 5461 A. Unless otherwise stated in the text, spectra refer to material at 20°. The experimental arrangements fall into three main classes: excitation by Hg 4358 A. using low-pressure arcs; excitation by Hg 5461 A. using low-pressure arcs; excitation by Hg 5461 A. using medium-pressure arcs.

Solutions of dinitrogen tetroxide in nitric acid absorb so strongly in the blue region that, in order to excite Raman spectra by Hg 4358 A., it was necessary to use a technique in which the paths of both incident and Raman radiations were as short as possible. This was achieved by using a rectangular, fused quartz cell of interior dimensions 2 × 40 × 14 mm. The construction of such a cell, and the method of mounting it on the axis of the collimator of the spectrograph, have been described by Poole (*J.*, 1946, 245). The incident radiation from a vertical, low-pressure, direct-current, mercury arc was focused by an F/1·5 lens on to a point near that end of the cell which was closer to the slit. The Raman radiation which had to traverse only a short path through the liquid was focused by a lens on the slit of the spectrograph. Using Ilford Special Rapid plates, and a slit width of 0·1 mm., a spectrum containing the main nitrate ion frequency was obtained from a 1% solution of dinitrogen tetroxide in nitric acid after an exposure of 170 hours.

The method used for the excitation of Raman spectra by Hg 5461 A., using low-pressure arcs, was similar to that described in Part I for liquids which are available in quantity and are not decomposed by the exciting radiation. The light from the source was approximately focused on the Raman cell by a cylindrical tube 3 cm. in diameter, which was filled with a 40% solution of a mixture of about equal quantities of neodymium and praseodymium chlorides. By using this filter in conjunction with 1 cm. of saturated copper chloride solution in a concentric, annular cell, arranged co-axially with the Raman cell, the spectral background was reduced, weak mercury lines removed, and the intensities of Hg 5770 A. and 5790 A. were reduced sufficiently to prevent halation on the photographic plate. In fact, under such conditions, these lines were sharp enough to be used as reference lines for measuring purposes.

Raman spectra have also been excited by Hg 5461 A., using 80-watt Osira mercury arcs. The intensity of Hg 5461 A. in the radiation from these arcs is much greater than that from the low-pressure arcs, but the line is also broader, and the spectral background in the region 5400—5600 A. is much higher. By using these arcs, it was possible to reduce considerably the exposure time required to obtain Raman spectra excited by Hg 5461 A., although this gain was accompanied by some loss in resolving power, and by difficulty in detecting lines at about 600 cm.$^{-1}$. Two "Osira" arcs were placed on each side of the Raman cell, which was 15 cm. long and 2 cm. in diameter. Filters of copper chloride and mixed neodymium and praseodymium chlorides were used as before. With this arrangement it was possible to record, on Kodak P 1200 plates, strong Raman spectra of even a 10% solution of dinitrogen tetroxide in nitric acid with an exposure of 24 hours.

The authors thank Professor C. K. Ingold, F.R.S., for his help and advice. They are indebted to the Department of Scientific and Industrial Research for a grant to one of them (J. D. S. G.).

WILLIAM RAMSAY AND RALPH FOSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1.

[*Received, December 17th*, 1949.]

512. *Kinetics and Mechanism of Aromatic Nitration. Part VI. The Nitration of Phenols and Phenolic Ethers: the Concomitant Dealkylation of Phenolic Ethers. The Role of Nitrous Acid.*

By C. A. Bunton, E. D. Hughes, C. K. Ingold, D. I. H. Jacobs, M. H. Jones, G. J. Minkoff, and R. I. Reed.

It has been shown (Parts I—V; *J.*, 1938, 929; 1950, 2400—2467) that the nitration of aromatic compounds in general by nitric acid in organic solvents is retarded by nitrous acid, the "zeroth-order" equation

$$\text{Rate} \propto [\text{ArH}]^0(a + b[\text{HNO}_2]^1[\text{H}^+]^1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(i)}$$

applying to sufficiently reactive aromatic compounds, when nitric acid is in constant excess. This law has been interpreted as characteristic of nitration by the free nitronium ion, which, however, may also enter reaction in combined forms, such as the nitric acidium ion, and the dinitrogen pentoxide molecule. Against this background, a special situation arises in the nitration of phenol and aniline and their derivatives, including the laterally alkylated derivatives. Such nitrations are known to be accelerated by nitrous acid, to involve kinetics that have hitherto defied analysis, to exhibit a tendency to the loss of a lateral alkyl group, and to involve other non-oxidative and oxidative side-reactions. These phenomena are here examined over the field of phenols and phenolic ethers.

The acceleration by nitrous acid is shown to be due to a special mechanism of nitration governed by the kinetic law

$$\text{Rate} \propto [\text{ArH}]^1[\text{HNO}_2]^1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(ii)}$$

nitric acid being in constant excess. The complex kinetics are due, generally and essentially, to the superposition of this special process on the general nitration process, which, for compounds as reactive as phenols and phenolic ethers, is governed by the zeroth-order equation (i).

The transition which replaces the special mechanism (ii) by the general mechanism (i) may be effected by increasing the nitric acid concentration, *i.e.*, the availability of nitronium ion, and by decreasing the nitrous acid concentration. In the nitration of *p*-chloroanisole by nitric acid in acetic acid, it was possible to isolate the pure special mechanism (ii), and to effect, as described, a complete mechanistic conversion to the pure general mechanism (i), rates throughout remaining within the range of magnitudes which allow kinetic measurement. In some other cases, rates get out of hand when a similarly complete demonstration is attempted: in general the mechanisms are superposed. For the nitration of *p*-nitrophenol in acetic acid, the pure special mechanism was isolated; but the transition to the general mechanism was followed only to the stage of giving to the latter a dominating, and not an exclusive, importance. In the nitration of anisole in acetic acid, neither mechanism could be obtained in a pure condition; but a shift was demonstrated from a strongly predominating special mechanism to a strongly predominating general mechanism. In the nitration of phenol in acetic acid, and in water, qualitatively similar shifts were realised.

A theory of the special mechanism is given: in it, the nitrosonium ion plays approximately the same part as the nitronium ion plays in the general mechanism. It is assumed that the special mechanism leads primarily to nitrosation, and that the formed nitroso-compounds are rapidly oxidised to nitro-compounds, thereby causing no net loss or gain of nitrous acid.

The nitrosonium ion is assumed to be capable of entering into reaction, not only in the free state, but also in combined forms, such as the nitrous acidium ion and the dinitrogen trioxide molecule. Changes are demonstrated in the *ortho*/*para*-ratio for the nitration of phenol in water, and in acetic acid, under various conditions, and are interpreted on these lines.

Phenolic ethers may be dealkylated during nitration. *p*-Chloroanisole is partly dealkylated on nitration by nitric acid in acetic acid, giving 4-chloro-2 : 6-dinitrophenol along with 4-chloro-2-nitroanisole. This is true for nitration alike by the pure special mechanism and by the pure general mechanism; but the proportion of dealkylation is greater for the special than for the general mechanism. For nitration by the special mechanism it was demonstrated that the proportion of dealkylation is characteristic: it remained constant over a 100-fold change in the reaction rate. These dealkylations involve no oxidation, and do not disturb the kinetic forms of nitration. Acetic acid being the solvent, the eliminated methyl group was recovered (60% yield) as methyl acetate.

It is assumed that in the course of the nitration an oxonium ion is formed, which loses a carbonium ion, CH_3^+, after the usual heterolytic pattern of 'onium ion decompositions. Unlike anisole and *p*-chloroanisole, 2 : 6-dichloroanisole and 2 : 6-dimethylanisole were not dealkylated during nitration: this is attributed to steric hindrance in the formation of the assumed oxonium ions.

Although oxidation is thus shown not to be necessary for the detachment of an alkyl group, not all dealkylations are free from oxidation. Thus the loss of the ethyl group during nitration of *p*-chlorophenetole involves much oxidation, with production of nitrous acid, which complicates the kinetics of the nitration.

Other non-nitrating side-reactions may occur, which depend on condensation through reactive nuclear positions to produce deeply coloured compounds, or on polycondensation to give tars, if there are several such positions. Such reactions may be non-oxidative or oxidative; in the latter event they produce autocatalysis or auto-retardation, according as the special

or general nitration mechanism is dominating. The main nuclear side-reaction accompanying the nitration of anisole has been studied. It is a non-oxidative condensation between anisole and nitrous acid, giving, in proportions of the order of 10%, under the conditions used, the coloured dianisyloxidoammonium ion, Ar_2NO^+.* This condensation with nitrous acid, like the nitration dependent on nitrous acid, is of first order with respect to anisole.

The only observed nitration mechanisms being the above-described general and special mechanisms, the question has been considered as to why, for phenol and aniline derivatives, the former tends to be replaced by the latter. It is concluded that in principle both mechanisms are universal, but that the special mechanism receives special advantages from the use of highly reactive aromatic compounds. The nitronium ion is a much more reactive substituting agent, but is also much more easily destroyed by bases, than is the nitrosonium ion. In order to secure only mononitration of a highly reactive aromatic compound, it is necessary strongly to restrict the nitronium ion supply by introducing bases such as water; and this leaves the field open for substitution by the nitrosonium ion. From the conclusion that the relevant peculiarity of phenol and aniline derivatives is simply their reactivity, it follows that the special mechanism of nitration should be observable with other kinds of aromatic compound, *e.g.*, hydrocarbons, if sufficiently reactive ones can be found. This has been demonstrated in the example of mesitylene. Complementing what was done with phenol derivatives, the pure general mechanism has, in this case, been made the starting point of a progressive mechanistic change, which has been followed until the special mechanism is in nearly complete control.

(1) *Background and Plan.*

(1.1) *The Special Nature of the Nitration of Phenol and Aniline.*—It has long been apparent that the nitration by nitric acid of phenol and aniline, and of their laterally alkylated derivatives such as anisole and mono- and di-methylaniline, pursues a mechanism which is essentially different from the mechanisms followed by the nitration of aromatic compounds in general.

The existence of the difference is strikingly attested by the effect of nitrous acid. The literature contains many records which show that nitrous acid is a positive catalyst for the nitration of those aromatic compounds of which phenol and aniline are the parents. In certain of these reactions nitrous acid is produced by a concurrent oxidation of the aromatic compound by the nitric acid: when this happens the nitrations are autocatalytic. On the other hand, nitrous acid is in general a negative catalyst for the nitration by nitric acid of aromatic compounds outside the limited class of phenol and aniline derivatives (cf. Part II, Section 4, *J.*, 1950, 2430).

Our study of the general mechanisms of aromatic nitration having developed as described in Parts I—V, we became interested in the nature of the special process operating in the nitration of derivatives of phenol and aniline, and in the reason why this special process appears to replace the ordinary process only for this particular group of aromatic compounds. These are the questions to be considered in Parts VI—VIII.

The previous literature gives two broad indications concerning the special process. The first is that nitrous acid plays a fundamental role. The positive catalysis by nitrous acid is often very strong, in contrast to the negative catalysis of the ordinary process, which is relatively weak, and has been shown (Part II, *loc. cit.*) to be incidental to the mechanism of nitration.

The second indication is of a basic similarity, despite the differences, between the special nitration process and the general one. This follows from the fact that the nitrations of derivatives of phenol and aniline obey the ordinary laws of orientation. This shows that the reagent in the special process, if not the nitronium ion, must at least be electrophilic, like the nitronium ion.

In this paper we describe experiments which were designed to elucidate the nature, and conditions of incursion, of the special process in so far as it applies to the nitration of derivatives of phenol. Derivatives of aniline are treated in the following papers.

(1.2) *Previous Work on the Mechanism of Nitration of Phenols and Phenolic Ethers.*—There is a considerable literature of previous attempts to elucidate the mechanism of nitration of this group of aromatic compounds. The rate of nitration of phenol by nitric acid in water was first examined by Martinsen (*Z. physikal. Chem.*, 1904, **50**, 385), who showed that the reaction was autocatalysed by the nitrous acid it produced, and indeed that, with nitric acid in only moderate concentration, the presence of nitrous acid was essential to the reaction.

Similar observations were made by Klemenc and his collaborators using ether as solvent (Klemenc, *Monatsh.*, 1914, **35**, 85; Klemenc and Ekl, *ibid.*, 1918, **39**, 641; Klemenc and Schöller, *Z. anorg. Chem.*, 1924, **141**, 231). Klemenc and Schöller attempted to analyse the kinetics of nitration in water and in ether. They gave approximate equations such as rate $\propto [HNO_3]^{3/2}[HNO_2]^{3/2}$ for water, and rate $\propto [HNO_3]^{3/2}[HNO_2]^{3/2}$ for ether. They supposed

* Here and in later parts of this paper, anisyl is used for the radical MeO·C_6H_4· and not for its benzyl analogue.

that the nitrating agent might be an acid $H_2N_2O_4$, and thought of the nitration process as a modified oxidation.

Arnall studied the nitration of phenol by nitric acid in ethyl alcohol, and again observed autocatalysis by the formed nitrous acid (*J.*, 1923, **123**, 3111; 1924, **125**, 811). Zawidski made similar experiments, and gave the approximate relation, rate $\propto [HNO_3][HNO_2]$ (*Rocz. Chem.*, 1925, **5**, 504). The mechanism of the reaction which Arnall suggested would now be called a homolytic process of nitration:

$$N_2O_4 + C_6H_5{\cdot}OH \longrightarrow NO_2{\cdot}C_6H_4{\cdot}OH + HNO_2$$

Kartaschev studied the nitration of phenol in water and in ethyl acetate (*J. Russ. Chem. Soc.*, 1927, **59**, 813, 833; 1930, **12**, 2129; Kartaschev and Sai-Moiseeva, *ibid.*, p. 385). Using Liebermann's test, he obtained indications of the presence of nitrosophenols in the early stages of nitration, and accordingly supported the theory that nitration proceeds through a nitrosation followed by an oxidation:

$$HNO_2 + C_6H_5{\cdot}OH \longrightarrow NO{\cdot}C_6H_4{\cdot}OH \xrightarrow{HNO_3} NO_2{\cdot}C_6H_4{\cdot}OH + HNO_2$$

Bunton, Hughes, Minkoff, and Reed have reported (*Nature*, 1946, **158**, 514) the isolation of some *p*-nitrosophenol from the product of an interrupted aqueous nitration of phenol.

Veibel has attempted to deal with the main difficulty which faced the theory that nitration proceeds through nitrosation, *viz.*, that the aqueous nitration of phenol produces a mixture of *o*- and *p*-nitrophenols containing a considerable excess of the former, whereas the nitrosation of phenols leads principally to the *p*-nitroso-compound (*Ber.*, 1930, **63**, 1577; *Z. physikal. Chem.*, 1930, *B*, **10**, 22). Veibel was the first to show that a little *o*-nitroso-compound is formed as well. He dealt with the remaining large discrepancy between the *o*/*p*-ratios for nitration and for nitrosation by supposing that phenol reversibly forms two intermediate molecular compounds with nitrous acid, one with the latter linked in the *ortho*-position, and the other with it attached to the *para*-position. He assumed that each of these compounds could yield either a nitrosophenol or a nitrophenol, of corresponding orientation, by alternative parallel modes of decomposition. By assigning suitable relative rates to the different hypothetical stages of reaction, the differing *o*/*p*-ratios could be accommodated.

Recently, Schramm and Westheimer have reported on the nitration of anisole in aqueous nitric acid (*J. Amer. Chem. Soc.*, 1948, **70**, 1782). They showed that nitrous acid was necessary for the reaction, and made it probable that nitroso-anisoles were intermediates, since *p*-nitroso-anisole gave similar end-products. These contained not only nitroanisoles, but also 2 : 4-dinitrophenols.

Partial dearylation of diaryl ethers during nitration has been reported by Reilly, Drumm, and Barrett (*J.*, 1927, 67). The partial dealkylation observed by Schramm and Westheimer in the nitration of anisole has been found by us to be a somewhat general accompaniment of the nitration of *O*-alkylated phenols. Dealkylation is again observed in the nitration of *N*-dialkylated anilines (cf. Part VII, *J.*, 1950, paper no. 513). We see in these facts another preliminary indication of major importance, *viz.*, that alkyl displacement from fully *O*- or *N*-alkylated derivatives of phenol or aniline is in some way concerned in the nitration mechanism which we are investigating.

(1.3) *Plan of the Present Work on the Nitration of Phenols and Phenolic Ethers.*—In this investigation much attention has been given to the task of isolating the nitration mechanism we wished to observe, from accompanying phenomena of less immediate interest. Some degree of isolation is necessary if conclusions are to be drawn from a study of reaction products, and a high degree of isolation is required if the method of chemical kinetics is to be used to the best effect. In this preliminary search for a suitable system, we found that some gain resulted from modifying the conditions of nitration, but much more from changing the substance nitrated. Thus we passed in succession from the study of the nitration of phenol, the most complicated case of all, to that of anisole, which is not much simpler, then to that of substituted phenols, and finally to substituted anisoles. We shall report our work in these fields in almost the reverse order, because it was from the investigation of substituted anisoles, the leading example being *p*-chloroanisole, that we obtained most insight into the reaction. With this information, it was possible to interpret kinetic results obtained earlier for substituted phenols, in particular, *p*-nitrophenol, and qualitatively to understand a number of kinetic and other observations which had been made on the nitration of anisole and phenol.

(2) *Products of Nitration of* p-*Chloroanisole.*

(2.1) *The Partial Demethylation accompanying Nitration.*—*p*-Chloroanisole is smoothly nitrated by 4—10M-nitric acid in acetic acid at temperatures between −15° and +35°. There is very little, if any, accompanying oxidation. It is possible to account for almost the whole of the introduced aromatic material in the form of two nitro-compounds, *viz.*, 4-chloro-2-nitroanisole and 4-chloro-2 : 6-dinitrophenol. The production of the latter involves elimination of the methyl group of *p*-chloroanisole. The fate of this group is established in Section 2.2.

We have determined the proportions in which 4-chloro-2-nitroanisole and 4-chloro-2 : 6-dinitrophenol are produced during the nitration of *p*-chloroanisole under various conditions. In order to understand the significance of the conditions, it is necessary to refer to some of the kinetic findings given in Section 3, especially to those which relate to effects of " nitrous acid " in the presence of different concentrations of nitric acid. Following Benford and Ingold (*J.*, 1938, 929), we shall mean by " nitrous acid " the total material in a nitration medium which, after dilution with water, could be estimated as nitrous acid.

A range of concentrations of nitric acid has been investigated. Over the lower part of the range, *i.e.*, from below 4M- to above 6M-nitric acid, the nitration is strongly catalysed by nitrous acid; but there is no autocatalysis, as there is with some phenol derivatives, and no nitrous acid is produced in the reaction, *i.e.*, there is no oxidation. In the lowest part of the concentration range, near 4M-nitric acid, the presence of nitrous acid is essential to give the reaction an appreciable rate. At higher concentrations, near 6M-nitric acid, there is a detectable reaction in the absence of nitrous acid; but still this material is a powerful catalyst, and the presence of quite a small amount will determine that nearly the whole observed reaction is catalysed. At still higher nitric acid concentrations the importance of the uncatalysed reaction increases, while that of the catalysed process diminishes. In the highest part of the investigated range, from 9M- to 10M-nitric acid, the reaction in the absence of nitrous acid becomes rapid; and now nitrous acid is found to be a negative catalyst. We shall later consider the other kinetic changes that occur concurrently with these, as well as the quantitative aspect of all these effects. The point now to be made is that our investigated range of concentrations includes (*a*) a region in which the reaction is wholly dependent on catalysis by nitrous acid, (*b*) a transitional region, and (*c*) a region in which nitration is, not merely not assisted, but is retarded, by nitrous acid. In region (*a*), the mechanism is obviously the special one, applying to the nitration of derivatives of phenol and aniline, which we are at present concerned to investigate; for the essential character by which we recognise it is its dependence on strong positive catalysis by nitrous acid. In region (*c*), the mechanism is, as we shall later fully confirm, the general mechanism of aromatic nitration, to the study of which Parts I and II were devoted, where the characteristic negative catalysis by nitrous acid was first demonstrated. The present importance of the transitional region (*b*) is simply that it guarantees for us a reasonably complete isolation of the special mechanism in region (*a*), from the general mechanism characteristic of region (*c*).

TABLE I.

Proportions of nitro-products formed by the nitration of p-*chloroanisole by nitric acid in acetic acid.*

Expt. no.	Temp.	HNO_2 (M.).	HNO_3 (M.).	CNA * (mols. %).	CDNP * (mols. %).	CNA / CDNP
302	20°	3·81	0·193	59·5	30·2	1·97
304, 311, 312	,,	4·75	high	60·7	29·9	2·03
305	,,	5·70	0·038	60·5	30·5	1·98
313—316	,,	,,	high	66·0	33·2	1·99
307	−10°	10·00	none	75·0	24·0	3·12

* CNA = 4-Chloro-2-nitroanisole; CDNP = 4-chloro-2 : 6-dinitrophenol.

The measured proportions of nitro-compounds are given in Table I. The experiments at 20°, with nitric acid in concentrations 3·81, 4·75, 5·70M., involve conditions (*a*), in which the mechanism dependent on catalysis by nitrous acid is dominating. Although the rates of nitration at exactly these concentrations and temperature were not measured, it can be estimated, from the kinetic measurements recorded in Section 3, that in the group of experiments now considered the reaction rates must have varied over a range of the order of 100-fold. The significant result is that, in spite of this, the ratio in which 4-chloro-2-nitroanisole and 4-chloro-2 : 6-dinitrophenol

are produced, *i.e.*, the proportion of demethylation, is practically constant. We conclude that, in the mechanism operating over this range of conditions, the processes of nuclear nitration and lateral demethylation either depend identically on a common reagent, or involve a common intermediate; and that the factors which control the rate of the total reaction affect either the rate, or the equilibrium degree, of formation of this reagent or intermediate, rather than the rate of its conversion into the products.

In the measurements at −10° with nitric acid in concentration 10·0M., the conditions are those labelled (*c*) above, and the mechanism of nitration is the ordinary one, involving attack by the nitronium ion. In this mechanism, nitrous acid is just a complication, and we record in Table I an experiment in which it was excluded. This shows that demethylation also occurs during nitration by the nitronium ion mechanism, although the proportion of demethylation is appreciably different from that applying to the nitration mechanism dependent on nitrous acid.

The following qualitative experiments were carried out in order to determine, or delimit, the reactants involved in demethylation. 4-Chloro-2-nitroanisole was neither demethylated nor further nitrated under the conditions of the experiments noted in Table I. 4-Chloroanisole was not demethylated by a large concentration of sulphuric acid in acetic acid; this makes it clear that no ordinary kind of acidolysis is involved. 4-Chloroanisole was demethylated by a solution of nitrosonium hydrogen sulphate ("nitrosylsulphuric acid") in acetic acid. It was also demethylated by a solution of redistilled dinitrogen tetroxide in acetic acid. In each case the aromatic product gave the reactions of nitrosophenols. With a solution of colourless anhydrous nitric acid, together with urea nitrate, in acetic acid, no reaction at all occurred, unless the concentration of nitric acid was high enough to bring about nitration; and then considerable demethylation accompanied the nitration.

We interpret these results as meaning that there are two demethylating agents, or types of demethylating agent. One is the nitrosonium ion, or a "carrier" of the nitrosonium ion. The other is the nitronium ion, or a "carrier" of the nitronium ion. In either case, the demethylating agent is apparently not effective for demethylation except when it is also effective for nitrosation or nitration. Thus the two processes are closely linked together. The ineffectiveness of sulphuric acid allows us to conclude that the hydrogen ion, and "carriers" of the hydrogen ion (*i.e.*, acids), are not responsible for the observed demethylations.

(2.2) *The Fate of the Eliminated Methyl Group.*—*p*-Chloroanisole was nitrated by a 4M-solution of nitric acid in acetic acid at 35°, these conditions ensuring that the nitration mechanism is the special one, depending on catalysis by nitrous acid. The eliminated methyl group was recovered in the form of methyl acetate (cf. Section 12. 2). No sign of any considerable degree of oxidation was observed.

Experiments on the nitration of *p*-chlorophenetole were carried out, the conditions being as described above; but ethyl acetate could not be isolated, although it was detected by its odour during the attempts which were made to separate it. In contrast to the nitration of *p*-chloroanisole, the nitration of *p*-chlorophenetole involves a considerable amount of oxidation. Blank experiments with added ethyl acetate, and also with added ethyl nitrate, showed that, had either of these esters been produced in any substantial proportion, it could have been isolated by the methods employed. It seemed clear from these results that the eliminated ethyl group had been converted into oxidised forms. Attempts to detect acetaldehyde were unsuccessful. The possible production of acetic acid could not be tested, owing to the use of this substance as solvent.

We conclude from these experiments that, although oxidation may accompany the elimination of an alkyl group during the nitration of a phenolic ether, oxidation is not essential for the detaching of the alkyl group. We consider that the production of methyl acetate in the experiments on the nitration of *p*-chloroanisole by nitric acid in acetic acid makes it certain that the methyl group of the phenolic ether separates as its cation CH_3^+. This cation is sufficiently resistant to the oxidising environment to terminate its existence in the normal way, *viz.*, by combination with the most freely available anion, which, in these experiments, is the acetate ion derived from the acetic acid solvent.

(3) *Kinetics of the Nitration of* p-*Chloroanisole.*

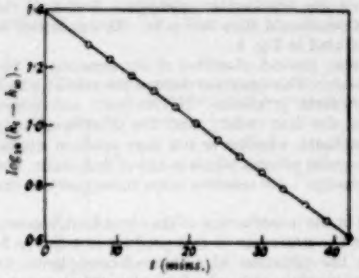
(3.1) *Constancy of the Nitrous Acid Concentration.*—The kinetics of nitration of *p*-chloroanisole by nitric acid in acetic acid, in the presence of what we are calling "nitrous acid," has been studied by our usual technique which employs the dilatometer as the main instrument, with chemical analysis as an occasional check. In this method, the nitrating acid is kept in large

excess (*e.g.*, 50-fold) over the aromatic compound, and the order of reaction with respect to the aromatic compound is established; it is usually first or zeroth, but may have intermediate values; if it is first or zeroth, the dependence of the corresponding rate constant on the concentration of the nitrous acid, and on that of the nitric acid, is explored.

This procedure assumes that the concentration of the nitrous acid and of the nitric acid remains steady during a run, a condition which is obviously satisfied to a close approximation in the case of the nitric acid. But the nitrous acid is often present in a concentration of the same order of magnitude as that of the aromatic compound, and hence it is necessary to test for the consumption or production of nitrous acid.

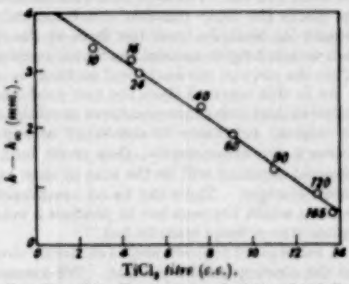
In the kinetic investigations of nitration which were reported in Parts I and II it was always found that the concentration of nitrous acid remained constant during a run. However, a corresponding result could not here be assumed, because we have present a different nitration mechanism. We find, nevertheless, that under the conditions of all the dilatometric runs reported below, the concentration of nitrous acid in the solution expelled from the dilatometer after reaction was the same as the concentration in the initial solution, to within the accuracy of analysis.

FIG. 1.



General kinetic form of the nitration of p*-chloroanisole in acetic acid by nitric acid in the concentration range* 4–6M.; *illustrated by Run No.* 353. *Temperature* 25·01°. *Initially,* $[HNO_3] = 4{\cdot}14$M.; $[HNO_2] = 0{\cdot}009$M.; $[Cl{\cdot}C_6H_3{\cdot}OMe] = 0{\cdot}031$M. *Finally,* $[HNO_2] = 0{\cdot}098$M. *First-order rate constant* $k_1 = 0{\cdot}000673$ *sec.*$^{-1}$.

FIG. 2.



Run No. 412: *Temperature,* 34·95°. *Initially,* $[HNO_3] = 4{\cdot}14$M.; $[HNO_2] = 0{\cdot}052$M., $[Cl{\cdot}C_6H_3{\cdot}OMe] = 0{\cdot}020$M. *The dilatometric readings are plotted against the chemical titres measuring the* 4*-chloro-*2*-nitroanisole in samples taken at the same times. The times (in minutes) are given by the figures against the graph. The slope of the curve corresponds to a titrimetric registration of the uptake of* 0·67 *mol. of nitroxyl per mol. of* p*-chloroanisole converted* (*cf. Table 1*).

The kinetics themselves, as reported below, confirm that nitrous acid is neither produced nor destroyed. For, under most of the conditions used, the rate depends strongly on the concentration of nitrous acid; and yet no signs were found either of an autocatalysis, or of any growing inhibition of the reaction.

(3.2) *The Nitrous Acid-catalysed Reaction. The Reaction Order with Respect to the Aromatic Compound.*—In this and the immediately following Sections we shall present data relating to the nitration of *p*-chloroanisole in acetic acid by means of nitric acid in the concentration range 4—6M., *i.e.*, under the conditions, labelled (*a*) in Section 2.1, in which the special nitration mechanism, dependent on nitrous acid, is in exclusive, or almost exclusive control.

For this range of concentrations of nitric acid, and, within it, for all investigated concentrations of nitrous acid (with a single exception to be mentioned in Section 3.3), the dilatometer rate followed the first-order rate law with considerable precision. In illustration Fig. 1 is given, in which the course of a run is shown in the form of a logarithmic plot of the variable part of the dilatometric height against the time.

The first-order character of the rate law was confirmed by carrying out two or more runs with the same nitrating solution, but with different initial concentrations of *p*-chloroanisole. Even though these concentrations might differ by several-fold, the first-order constants remained substantially the same. For example, the run, No. 353, illustrated in Fig. 1 was duplicated, and

in the duplicate, No. 354, the initial concentration of *p*-chloroanisole was made 2·7 times larger; however, the rate constant was the same :

Conditions as under Fig. 1, apart from initial [Cl·C_6H_4·OMe] :

No. 353. Initial Cl·C_6H_4·OMe = 0·031M.; k_1 = 0·000673 sec.$^{-1}$.
No. 354. ,, ,, = 0·082M.; k_1 = 0·00068 ,,

It was necessary to show that the dilatometric contractions are correlated with nitration of the aromatic molecule. This was done by following the same run dilatometrically and by chemical analysis. The analytical method involved separating 4-chloro-2-nitroanisole by solvent extraction from basified samples of the reaction solution, and then estimating nitroxyl in the extracted material by reduction with titanous chloride. The dilatometric and analytical rate constants agreed to within the rather large error of the analytical method, as the following comparison illustrates :

No. 412. Conditions as under Fig. 2 :
By dilatometry, k_1 = 0·000206 sec.$^{-1}$. By analysis, k_1 = 0·00023 sec.$^{-1}$.

The same run can be used to illustrate another form of comparison, which was sometimes made. One starts the same reaction simultaneously in a dilatometer and in a flask, and withdraws samples for analysis from the flask at the times of the dilatometer readings. A plot of the dilatometric heights against the titanous chloride titres should then be linear. It was linear, to within the error of the analytical method, as is illustrated in Fig. 2.

As in this reaction there are two products, we may remind ourselves of the meaning of the measured first-order rate constants in relation to them. This constant defines the rate at which the original substance is converted into its immediate products. If two such conversion processes run concurrently, they must both be of the first order; and the dilatometrically measured constant will be the sum of their rate constants, whether or not they produce similar volume changes. There can be no concurrent conversion process which is not of first order, not even one which happens not to produce a volume change. All reaction steps subsequent to the original step or steps must be fast.

A subsequent reaction step is evidently involved in the introduction of the second nitro-group into the dinitrophenolic product. We assume that the precursor of this product is 4-chloro-2-nitrophenol; and we have directly verified that the nitration of 4-chloro-2-nitrophenol to 4-chloro-2 : 6-dinitrophenol is a much faster reaction than the nitration of *p*-chloroanisole, under the conditions of the measurements.

(3.3) *The Nitrous Acid-catalysed Reaction (continued). The Reaction Order with Respect to Nitrous Acid.*—This was investigated by carrying out " blocks " of runs at a common temperature, with the same concentration of nitric acid in the acetic acid solvent, but with different concentrations of nitrous acid, the object being to find a relationship between the first-order rate constants and the nitrous acid concentrations. The results obtained in such a block of runs, applying to one of the lowest of the investigated concentrations of nitric acid, are given in Table II. It will be noticed that, with this concentration of nitric acid, when the content of nitrous acid is too small to be measured, then the reaction rate is too small to be observed. The empirical relation between the rate constant and the nitrous acid content is shown graphically in Fig. 3.

TABLE II.

Nitration of p*-chloroanisole in acetic acid by nitric acid in relatively low concentration. Dependence of the first-order rate constants* (k_1 *in sec.*$^{-1}$) *on the concentrations of nitrous acid.*

Temp. : 25·01°. $[HNO_3]$ = 4·14M. Initially [Cl·C_6H_4·OMe] ≈ 0·05M.

Run no.	358	357	355	363	361	364	367	366	365
$[HNO_2]$	0·000	0·041	0·073	0·110	0·133	0·165	0·237	0·278	0·338
10^4k_1	0·00	1·70	3·6	5·4	8·0	9·8	12·8	15·0	17·4

The results for another block of runs are given in Table III. They apply to a concentration of nitric acid which is near the upper limit, above which it would not be possible to say that only the nitration mechanism dependent on nitrous acid is under observation. Indeed, we see the first signs here that this mechanism is going to be superseded at still higher concentrations of nitric acid. For in this series, when the concentration of nitrous acid is reduced below the limits of detection, the reaction still has a measurable rate; and, moreover, this residual reaction is

not of first order with respect to the aromatic compound. In most of the experiments, however, the residual reaction is overlaid by the much faster catalysed reaction, which certainly is of first order with respect to the aromatic compound. Its rate constants are graphically compared with the corresponding nitrous acid concentrations in Fig. 4.

TABLE III.

Nitration of p*-chloroanisole in acetic acid by nitric acid at an intermediate concentration. Dependence of the first-order rate constants* (k_1 *in sec.*$^{-1}$) *on the concentrations of nitrous acid.*

Temp.: 25·01°. $[HNO_3] = 5{\cdot}94$M. Initially $[Cl{\cdot}C_6H_4{\cdot}OMe] \approx 0{\cdot}05$M.

Run no.	375	374	371	370	373	361	372
$[HNO_2]$	0·000	0·0057	0·032	0·046	0·080	0·097	0·141
10^4k_1	(1·8) *	8·8	18·7	31·6	50·2	58·1	79·3

* This was not a first-order reaction, but was a somewhat imperfect zeroth-order reaction. The figure in parentheses is its initial rate, calculated as for a first-order reaction, *i.e.*, expressed as the mol.-fraction converted per second. It is included in the Table only for the purpose of conveying a rough idea of how fast the uncatalysed reaction proceeds in these conditions, relatively to the truly first-order catalysed reactions.

The most significant result of this group of experiments will be obvious from Figs. 3 and 4: within the range of nitric acid concentrations 4—6M., the first-order rate constant for the

FIG. 3.

Dependence on nitrous acid concentration of the first-order rate constants for the nitration of p*-chloroanisole in acetic acid by nitric acid in two concentrations at 25·0°.*

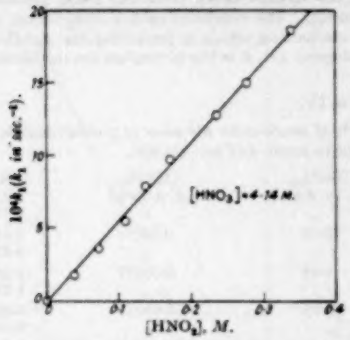
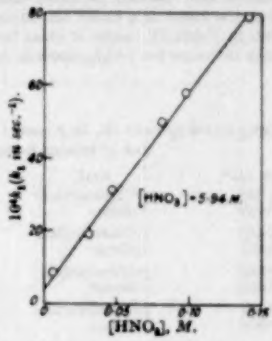


FIG. 4.



nitration of *p*-chloroanisole is proportional to the first power of the concentration of nitrous acid.

For a given nitrous acid concentration, the rate increases as the sixth-to-seventh power of the nitric acid concentration, within the range of concentrations now considered. Of course, the precise power has no simple chemical significance at these high concentrations.

We may summarise the above kinetic results for the nitration of *p*-chloroanisole by 4—6M-nitric acid in acetic acid. Writing ArH for *p*-chloroanisole and HNO_2 for what we have been calling " nitrous acid," the conclusion is as follows:

$$\left\{\begin{array}{l}\text{Rate} \propto [ArH][HNO_2] \\ \text{Rate increases steeply with } [HNO_3]\end{array}\right. \quad (HNO_3 \text{ in excess})$$

Near 6M-nitric acid it is a necessary condition for these kinetics that the concentration of nitrous acid shall not be too small.

In Section 6 we shall again illustrate the law Rate $\propto [ArH][HNO_2]$, this time for the nitration of a free phenol, rather than a phenolic ether. However, an exploratory kinetic examination of the nitration of a number of phenolic ethers and free phenols has convinced us that *this is a limiting law*. We have never observed the rate to vary as a higher power of the nitrous acid concentration than the first power (and neither has any previous investigator),

though it has often been found to vary as lower and non-constant powers, even negative powers. Furthermore, when the order with respect to nitrous acid falls below first-order, then the order with respect to the aromatic compound may also fall below first-order. The general kinetic picture is therefore complicated, but we can most easily discover the elements of which it is composed by progressively changing the conditions so that we pass from the domain of control by the limiting law already illustrated, through the region of complicated kinetics, to a situation in which a *second limiting law* is in control. The elucidation of this second law is the subject of the next two Sections.

(3.4) *The Nitrous Acid-anticatalysed Reaction. Reaction Order with Respect to the Aromatic Compound.*—In the example of the nitration of *p*-chloroanisole, the transition from the first limiting law to the second is made essentially by increasing the concentration of nitric acid. With nitric acid in 6—9M-concentration we encounter complicated kinetics with fractional, non-constant reaction orders. In the range 9—10M-nitric acid, simple kinetics are again observed. Near 9M-nitric acid, it is a condition that the concentration of nitrous acid shall not be too large. Above 10M-nitric acid, the reactions are too fast to be conveniently studied by our methods.

These nitrations were found to be of zeroth order with respect to the aromatic compound. A typical reaction–time curve, as observed dilatometrically, is shown in Fig. 5.

Hughes, Ingold, and Reed (cf. Part II) measured the zeroth-order rates of nitration of toluene, ethylbenzene, *p*-xylene, and mesitylene by nitric acid in acetic acid. It is readily possible to establish that the reaction mechanism which is yielding the zeroth-order nitration of *p*-chloroanisole by 9—10M-nitric acid in acetic acid is identical with that from which Hughes, Ingold, and Reed obtained zeroth-order kinetics, and proved to be the nitronium ion mechanism. One has simply to make a comparison of the absolute rates of nitration of *p*-chloroanisole and one of the other group of substances, say, toluene; all those aromatic compounds that obey the zeroth-order law, should, provided that that law always arises from the same mechanism, nitrate at the same rate under the same conditions. The results of such a comparison, which are given in Table IV, make it clear that the mechanism which is producing the zeroth-order kinetics is the same for *p*-chloroanisole as for toluene; *i.e.*, it is the nitronium ion mechanism.

TABLE IV.

Comparison of rates (k_0 *in g.-mol. l.*$^{-1}$ *sec.*$^{-1}$) *of zeroth-order nitration of* p-*chloroanisole and of toluene by nitric acid in acetic acid at* −14·93°.

Run no.*	ArH.	$[HNO_3]$.	$[HNO_2]$.	10^4k_0.
648	*p*-Chloroanisole	*ca.* 9·05	*ca.* 0·00035	9·12
649	Toluene	,,	,,	9·19
650	*p*-Chloroanisole	9·05	0·00070	9·95
651	Toluene	,,	,,	9·67
652	*p*-Chloroanisole	9·05	0·00077	9·26
653	Toluene	,,	,,	9·98
654	*p*-Chloroanisole	9·05	0·00076	9·65
655	Toluene	,,	,,	9·78

* The braces indicate pairs of runs with the same nitration medium.

It will already be clear that *p*-chloroanisole is reacting, in the conditions described, by the nitronium ion mechanism, which was elucidated, for aromatic nitration in general, in Part II. In organic solvents, and with nitric acid in constant excess, this mechanism led to two limiting forms of kinetics: sufficiently reactive aromatic compounds nitrated according to a zeroth-order law, this being one of the most characteristic kinetic features of the mechanism; and sufficiently unreactive aromatic compounds nitrated according to a first-order law. Since the methoxyl group is strongly activating in electrophilic substitution, while the chlorine substituent is only moderately deactivating, it is entirely consistent that *p*-chloroanisole should take its place with the group of reactive aromatic compounds which exhibit zeroth-order kinetics under the conditions specified.

With nitric acid in concentrations near 9M., the zeroth-order kinetic form of nitration is not sensibly disturbed by the presence of nitrous acid in concentrations up to 0·001M., although the actual rate of nitration is appreciably changed. However, large concentrations of nitrous acid, *e.g.*, 0·1M., disturb the kinetic order as well as increasing the reaction rate. This is obviously due to the incursion of the nitrous acid-catalysed mechanism, with its different form of dependence of the rate on the concentration of the aromatic compound. With somewhat

higher concentrations of nitric acid the faster zeroth-order reactions will tolerate more nitrous acid before they begin to lose their simple kinetic form.

(3.5) *The Nitrous Acid-anticatalysed Reaction (continued). Dependence of the Rate on Nitrous Acid.*—One of the characteristic features of nitration by the nitronium ion mechanism is that the rate of reaction is depressed by nitrous acid. Benford and Ingold (Part I) gave a law for the depression, *viz.*, that the reciprocal of the rate increases linearly with the square-root of the concentration of nitrous acid; and Hughes, Ingold, and Reed (Part II) confirmed the law, showing that it applied alike to zeroth-order and first-order reactions, and to the solvents nitromethane and acetic acid.

The effect of nitrous acid on the zeroth-order rate of nitration of *p*-chloroanisole by approximately 9M-nitric acid in acetic acid has been investigated within the range of concentrations of nitrous acid over which the zeroth-order law is preserved. The figures for a block of runs are given in Table V.

TABLE V.

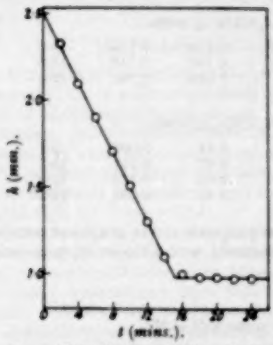
Nitration of p*-chloroanisole in acetic acid by nitric acid in one of the higher concentrations. Dependence of the zeroth-order rate constant* (k_0 *in sec.*$^{-1}$ *g.-mol. l.*$^{-1}$) *on the concentration of nitrous acid.*

Temp. −5·10°. $[HNO_3]$ = 9·05M. Initially $[Cl{\cdot}C_6H_4{\cdot}OMe] \approx 0{\cdot}02$M.

Run no.	392	385	391	386	389	388	387
$[HNO_2]$	0·0000	0·00025	0·00035	0·00055	0·00060	0·00075	0·00095
10^4k_0	0·35	0·24	0·22	0·20	0·21	0·19	0·17

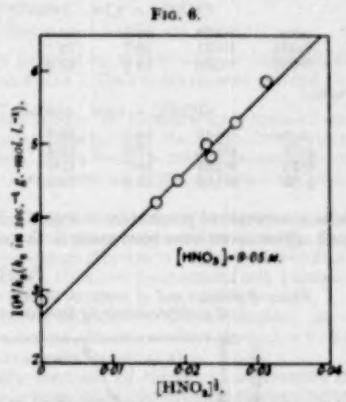
A plot of the reciprocal of the zeroth-order rate constant against the square root of the concentration of nitrous acid is shown in Fig. 6, from which it is clear that the law characteristic

FIG. 5.



General kinetic form of the nitration of p*-chloroanisole in acetic acid by 9—10*M*-nitric acid and in the absence of too large amounts of nitrous acid: illustrated by Run No.* 382. *Temperature* −11·21°. $[HNO_3]$ = 9·05M. $[HNO_2]$ = 0·000M. *Initially,* $[Cl{\cdot}C_6H_4{\cdot}OMe]$ = 0·020M. *Zeroth-order rate constant* k_0 = $0{\cdot}22 \times 10^{-4}$ *sec.*$^{-1}$ *g.-mol. l.*$^{-1}$.

FIG. 6.



Dependence on nitrous acid concentration of the zeroth-order rate constants for the nitration of p*-chloroanisole by 9·05*M*-nitric acid in acetic acid at* −5·10°.

of aromatic nitration by the nitronium ion mechanism is obeyed. This confirms the already drawn conclusion that the general mechanism of aromatic nitration is under observation in these experiments. This general mechanism provides the second limiting kinetic law:

$$\text{Rate} = [ArH]^0(a + b[HNO_2]^{1/2})^{-1}$$

The kinetic complications to which reference was made earlier arise from the superposition of

the special and the general mechanism, and from their very different forms of dependence of the rate on the concentrations of the aromatic compound, and also of the nitrous acid.

(3.6) *The Nitrous Acid-catalysed Reaction (continued from Section* 3.3). *Dependence of the Rate on Added Alkali-metal Nitrates and on Added Water.*—A short investigation has been made of the effect of the added substances mentioned on the rate of nitration of *p*-chloroanisole by the special mechanism, which acts to the exclusion of the general mechanism at the lower concentrations of nitric acid. In these experiments, nitrous acid has to be present. It is difficult to standardise its concentration over a series of runs intended to be comparative. However, a basis for measuring and comparing the kinetic effects of the added substances exists in the second-order constants, k_2 in the equation, rate $= k_2[\mathrm{ArH}][\mathrm{HNO_2}]$. These second-order constants are obtained by dividing the dilatometrically measured first-order constant, k_1, of each run by the concentration of nitrous acid which was present during that run.

Data showing the kinetic effect of added lithium nitrate, potassium nitrate, and water on the nitration of *p*-chloroanisole by approximately 4M-nitric acid in acetic acid are given in Table VI.

TABLE VI.

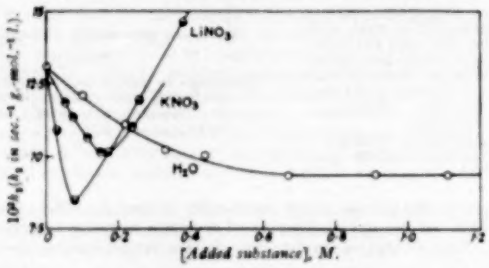
Effect of added substances ("AS") on the second-order rate constants (k_2 in sec.$^{-1}$ g.-mol.$^{-1}$ l.) for the nitration of p*-chloroanisole by* 4M*-nitric acid in acetic acid in the presence of nitrous acid at* 34·98°.

Run no.	[AS].	$[HNO_2]$.	10^4k_1.	10^3k_2.	Run no.	[AS].	$[HNO_2]$.	10^4k_1.	10^3k_2.
Added lithium nitrate:		($[HNO_2]$ = 4·2M.	Initially, $[Cl{\cdot}C_6H_4{\cdot}OMe] \approx 0.06$M.)						
453	none	0·079	12·6	15·9	456	0·162	0·074	9·2	12·4
458	0·040	0·067	8·9	13·3	455	0·244	0·071	10·3	14·5
460	0·081	0·041	4·2	10·3	454	0·385	0·065	11·5	17·7
Added potassium nitrate:		($[HNO_2]$ = 4·1M.	Initially $[Cl{\cdot}C_6H_4{\cdot}OMe] \approx 0.06$M.)						
443	none	0·158	22·0	14·0	445	0·114	0·134	15·0	11·2
446	0·055	0·131	16·7	12·7	448	0·152	0·119	13·0	10·9
447	0·076	0·108	13·3	12·2	450	0·228	0·102	12·0	11·8
Added water:		($[HNO_2]$ = 4·0M.	Initially $[Cl{\cdot}C_6H_4{\cdot}OMe] \approx 0.06$M.)						
496	none	0·148	19·4	13·1	500	0·44	0·090	9·1	10·1
497	0·11	0·141	17·0	12·1	507	0·67	0·141	13·1	9·3
498	0·22	0·134	14·7	11·1	509	0·89	0·132	12·3	9·3
499	0·33	0·131	13·4	10·2	510	1·11	0·131	12·2	9·4

The results are compared graphically in Fig. 7. For the purposes of the graphical comparison, some small adjustments have been made to the rate constants of the blocks of runs concerned

FIG. 7.

Effect of nitrates and of water on the rate of the nitrous acid-catalysed nitration of p*-chloroanisole by* 4M*-nitric acid in acetic acid at* 35°.



with the effect of salts, in order to bring them into correspondence, as regards the exact concentration of nitric acid, with the block of runs concerned with the effect of water.

Because of our lack of detailed knowledge concerning the condition of the added solutes in this type of medium, it is possible to offer only a qualitative and general interpretation of these results. The alkali-metal nitrates would appear to have two qualitatively opposite kinetic effects, which work according to different mathematical laws, and thus, by superposition, produced rate minima. The retarding effect, which dominates at the lower concentrations, we take to be a specific nitrate ion effect, and we suggest that it operates by repressing the dissociation of dinitrogen tetroxide into nitrosonium and nitrate ions (cf. Section 10). If this is true, it would seem to follow that the salts can be only partly ionised, since lithium and potassium nitrates give different depressions of reaction rate. The accelerative effect of the salts, which is the predominating effect at the higher salt concentrations, we believe to be a general salt effect, *i.e.*, an effect of ions or ion-pairs acting mainly electrostatically on some critical reaction stage, which again may be the ionisation of dinitrogen tetroxide.

The retarding effect of water is weaker than that of the salts; and most of the observed effect is exerted in the early stages of the progressive addition of water. We know that when a small amount of water is added to an excess of nitric acid, it combines, first, with any nitronium ion present to form nitric acidium ion, secondly, with nitric acid molecules to form a non-ionised hydrate, and thirdly, with protons from nitric acid to leave free nitrate ions (Gillespie and Millen, *Quart. Reviews*, 1948, **2**, 277; Part II, *J.*, 1950, 2400; Gillespie, Hughes, and Ingold, *J.*, 1950, 2473; Ingold and Millen, *J.*, 1950, 2612). In organic solvents such as acetic acid, the proportion of free nitronium ion is small (Part II, *loc. cit.*); and so we suppose that the main kinetic effects of water, in so far as they are exerted on the nitrosonium ion indirectly through their action on the nitric acid, are due to the second and third of the processes mentioned. The hydration of nitric acid molecules is certain to affect their power of promoting the ionisation of dinitrogen tetroxide; and the production of any free nitrate ion will repress nitrosonium ion formation as already described. Apart from these indirectly exerted effects, water may act directly on what we call " nitrous acid " by combining with its most reactive component, the nitrosonium ion, to give less reactive entities, such as the nitrous acidium ion and the nitrous acid molecule (cf. Part II, *loc. cit.*).

(4) *Products of Nitration of Simple and Substituted Anisoles.*

In this Section we shall note the products obtained by the nitration of four phenolic ethers under conditions of positive catalysis by nitrous acid. The results present contrasts which we believe to be theoretically significant.

Schramm and Westheimer have shown that anisole, on nitration by nitric acid containing nitrous acid in water as solvent, undergoes partial demethylation (*loc. cit.*). In our experiments, which have been conducted with acetic acid as the solvent, considerable amounts of deeply coloured and tarry by-products were formed; our recoveries of simple nitro-compounds seldom exceeded 80% (cf. Section 12.4).

p-Chloroanisole is nitrated more slowly than anisole by nitric acid in the lower of the investigated concentrations, *e.g.*, 4M., in acetic acid solutions containing nitrous acid. As we have shown, a considerable amount of demethylation occurs (Section 2). The total nitration is much more nearly quantitative than that of anisole. Coloured by-products are formed in small amount.

2 : 6-Dichloroanisole nitrates much more slowly still under similar conditions. In this case, scarcely any demethylation accompanies the nitration, the sole product of which is 2 : 6-dichloro-4-nitroanisole. Strongly coloured by-products are not formed at all.

2 : 6-Dimethylanisole nitrates more rapidly than any of the above compounds in similar conditions. Again, scarcely any demethylation takes place, the uniform product being 4-nitro-2 : 6-dimethylanisole. Again, deeply coloured by-products do not appear.

We conclude from these results that 2 : 6-disubstitution in a phenolic ether suppresses the dealkylation which otherwise would be liable to accompany nitration. The effect is not correlated with the general vigour of the reaction. It is not an indirect effect, arising from an increased tendency to reaction in the aromatic nucleus. We shall suggest (Section 10) that it is to be interpreted as an effect of the steric inhibition of an addition process essential to the demethylation. The formation of coloured products is discussed in Section 8.

(5) *Nitration of Anisole. Kinetics.*

The nitration of anisole by nitric acid in acetic acid containing nitrous acid has been investigated at temperatures near 20°, with nitric acid concentrations in the range 3—8M., and nitrous

acid concentrations varying in order of magnitude from 0·01 to 1·0M. The dilatometric method was again employed; and it was checked as usual by chemical analysis.

The kinetics are very complicated, and only the salient qualitative features will be described. However, these will be sufficient to enable us, in the light of our already gained knowledge, to recognise the principal elements which compose the complex situation. We might have expected complicated kinetics for the understood reason that the general and the special mechanism of nitration, which have completely different kinetics, are likely to be superposed. We shall find that the superposition of mechanisms does, indeed, dominate the kinetic picture. Moreover, some special sources of complication arise additionally to any encountered hitherto.

We are forewarned of such special effects by our knowledge that anisole, unlike *p*-chloroanisole, is not converted nearly quantitatively into simple nitration products, proportions of the order of 10% being simultaneously transformed into complex substances. Probably in part, though certainly not wholly, the production of these complex materials involves oxidation. From the point of view of reaction kinetics, the main extra complication appears in the form of an auto-catalysis, or in some cases an auto-retardation; such effects were never observed with *p*-chloroanisole. Under many of the conditions employed in the present nitrations of anisole, a proportion of this substance becomes oxidised, with the production of nitrous acid often in quantity much greater than that which was present initially; and this leads to autocatalysis, if the concentration of nitric acid is not too high, or to an auto-retardation, if the concentration of nitric acid is sufficiently high.

Autocatalysis has been observed in nitrations of anisole in acetic acid by nitric acid in the range of concentrations 3·0—6·0M. The chief additional condition for autocatalysis seems to be that the initial concentration of nitrous acid shall be low: usually it must be below 0·01M. This is not merely in order that the produced nitrous acid shall not be negligible in comparison with the initially present nitrous acid. The curious observation was repeatedly made that, once autocatalysis sets in, the nitrous acid may rise to considerably higher concentrations than those which, if they had been present initially, would have prevented any development of autocatalysis. The cause of this phenomenon is not known. Auto-retardation, again associated with the production of nitrous acid by oxidation, arises in the presence of higher concentrations of nitric acid, again provided that the initial concentration of nitrous acid is low.

For the next few paragraphs, we shall restrict description to those experiments in which a sufficient initial concentration of nitrous acid was employed to avoid the onset of autocatalysis or auto-retardation. In such cases the concentration of nitrous acid remained substantially constant during any one run. As usual, the nitric acid was in large and constant excess, so that the only reactant whose concentration varied during a run was the anisole.

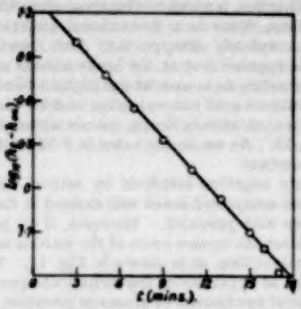
The order of reaction with respect to the anisole was not observed to have any exact and universal value; but it can fairly be described as being nearer to unity than to any other integral value over most of the conditions of the present survey. It is close to unity at the lower end of the investigated range of concentrations of nitric acid; it tends to fall, and to deviate more from constancy, at the upper end of the range. It is also very much closer to unity when the concentration of nitrous acid is high than when it is relatively low. The logarithmic plot of the course of a run with a high concentration of nitrous acid, and a relatively low concentration of nitric acid, is shown in Fig. 8.

We have calculated mean first-order rate constants for most of the runs carried out with anisole, even when the first-order law is not accurately obeyed. When it is not, the derived constants naturally have no exact meaning; but they do enable the rates of different runs to be compared in an approximate way: and such a comparison is necessary if we are to make even a qualitative appraisal of the main features of the effect of nitrous acid on the reaction rate. We shall now describe this effect in outline.

Over the range 3—6M. of nitric acid concentrations, the nitration is positively catalysed by nitrous acid. This is illustrated in Fig. 9 by reference to a block of nitrations in 4·93M-nitric acid. The diagram is a plot of the logarithm of the mean, first-order rate constant against the logarithm of the concentration of nitric acid. The points are seen approximately to define a straight line of positive slope. If the rate were proportional to the concentration of nitrous acid the slope would be unity; but in fact it is smaller, and corresponds to a rate proportional to the square-root of the concentration of nitrous acid. However, it is only accidental that the relevant power of the concentration of nitrous acid has in this case the simple value one-half.

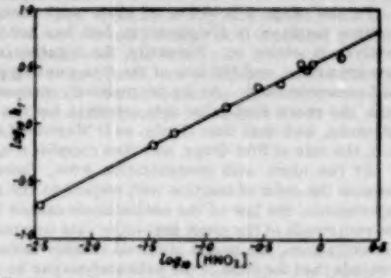
If, over the range 3—6M. of nitric acid concentrations, we represent the dependence of the rate on the nitrous acid concentration by an approximate power of the latter, as has just been

FIG. 8.



First-order nitration of anisole by nitric acid in acetic acid containing a high concentration of nitrous acid: illustrated by Run No. 145. *Temperature* 20·87°. $[HNO_3] = 4{\cdot}93$M. $[HNO_2] = 0{\cdot}691$M. *Initially* $[PhOMe] = 0{\cdot}026$M. *Rate constant* $k_1 = 0{\cdot}00414$ *sec.*$^{-1}$.

FIG. 9.



Positive catalysis in the nitration of anisole by 4·93M-*nitric acid in acetic acid containing nitrous acid at* 19·97°. *Dependence of the rate on the concentration of nitrous acid. The logarithms of the mean first-order rate constants are plotted against the logarithms of the nitrous acid concentrations. The slope of the line is* +0·50.

FIG. 10.

Negative and positive catalysis by nitrous acid of the nitration of anisole by 6·30M-*nitric acid in acetic acid at* 19·97°. *The mean first-order rate constants are plotted against concentrations of nitrous acid.*

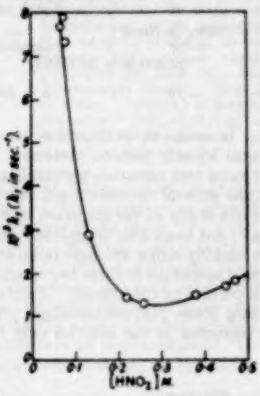
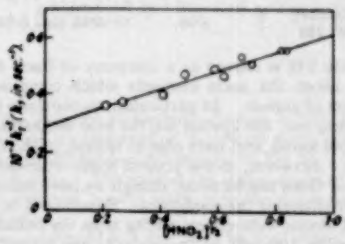


FIG. 11.

Negative catalysis by nitrous acid of the nitration of anisole by 8·0M-*nitric acid in acetic acid at* 19·97°. *The reciprocals of the mean first-order rate constants are plotted against the square-roots of the nitrous acid concentrations.*



illustrated for nitrations in 4·93M-nitric acid, then this power drops throughout the concentration range as follows:

$[HNO_3]$	3·00	4·93	5·20	6·00
Power of $[HNO_3]$	0·65	0·5	0·35	0·2

Even in 3M-nitric acid there is no close approach to a reaction of unit order with respect to nitrous acid, such as would indicate an isolation of the special mechanism of nitration. And it is clear

from the trend of the figures that, in nitric acid of concentrations above 6M., positive catalysis by nitrous acid, the main characteristic of the special mechanism, is going to disappear altogether.

In the range 6·3—6·7M. of nitric acid concentrations, there is a transitional situation : positive catalysis is disappearing, but has not quite completely disappeared; and negative catalysis is setting in. Naturally, the negative catalysis appears first at the lower nitrous acid concentrations, and the last of the disappearing positive catalysis is seen at the highest nitrous acid concentrations. As we progressively increase the nitrous acid concentration in 6·3M-nitric acid, the mean first-order rate constant for the nitration of anisole drops, passes through a minimum, and then rises slowly, as is illustrated in Fig. 10. As we do the same in 6·72M-nitric acid, the rate at first drops, and then remains roughly constant.

At the nitric acid concentration 8·0M., there is only negative catalysis by nitrous acid. Because the order of reaction with respect to the aromatic compound is not well defined in these experiments, the law of the anticatalysis cannot be given with precision. However, if we plot the reciprocals of the mean first-order rate constants against the square-roots of the nitrous acid concentrations, the points obtained roughly define a straight line, as is shown in Fig. 11. We conclude that the form of the anticatalysis can be regarded as approaching the reciprocal-square-root law, which characterises the anticatalysis of the general mechanism of aromatic nitration.

TABLE VII.

Summary of the main features of the kinetics of the nitration of anisole by nitric acid in acetic acid containing nitrous acid at 20°.

Run no.	$[HNO_3]$.	$[HNO_2] = a$.	Type of catalysis by HNO_2.	Rate approx. propl. to :
189—196, 203	3·00	Initial $a<0·01$	+ Auto. (a rises)	—
		$0·02<a<0·25$	+ ve	$a^{0·46}$
137—147	4·93	$0·01<a<1·25$	+ ve	$a^{0·5}$
198—204, 206, 207	5·20	Initial $a<0·01$	+ Auto. (a rises)	—
		$0·02<a<0·50$	+ ve	$a^{0·31}$
220—228	6·00	$0·02<a<0·25$	+ ve	$a^{0·5}$
229—248	6·30	Initial $a<0·02$	± Auto. (a rises)	—
		$0·05<a<0·25$	− ve	(complicated)
		$0·25<a<0·50$	+ ve	(weak effect)
159—167	6·72	Initial $a<0·20$	− Auto. (a rises)	—
		$0·05<a<0·50$	− ve	(complicated)
		$0·05<a<1·25$	(practically no effect)	
178—187, 266, 268	8·00	$0·04<a<0·75$	− ve	$(a + ba^{1/2})^2$

Table VII is offered as a summary of these findings. It seems to us that they leave little doubt about the main elements which compose the total kinetic picture presented by the nitration of anisole. In particular, we conclude that the same two nitration mechanisms are in operation, *viz.*, the special nitrous acid mechanism, and the general nitronium ion mechanism, which we found, and were able to isolate, in the course of our study of the nitration of *p*-chloro-anisole. However, in the present study of anisole we have not been able completely to isolate either of those mechanisms, though we have succeeded in making either strongly dominating by suitably changing the conditions. Superposed on the normal operation of these two mechanisms, we find kinetic auto-effects arising from the oxidation of a portion of the anisole. Furthermore, appreciable amounts of by-products are formed, including some polycondensation products. These are extra complexities; but in spite of them, we recognise in the kinetics only the two mechanisms of nitration specified above.

(6) *Nitration of* p-*Nitrophenol. Kinetics.*

(6.1) *Preliminary Observations.*—The rate of nitration of *p*-nitrophenol by nitric acid in acetic acid containing nitrous acid has been studied at temperatures near 20° over the range of concentrations 1·4—10·0M. of nitric acid, and with nitrous acid concentrations varying from values of the order of 0·01M. to values of the order of 1·0M.

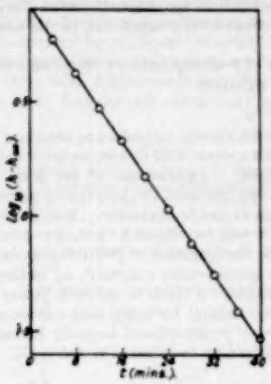
Our usual dilatometric technique has been employed. It was proved by chemical examination that the reaction measured by the dilatometric contraction in these experiments consists in the conversion of the *p*-nitrophenol into the single product 2 : 4-dinitrophenol. No

by-products of any kind are formed in appreciable quantity, and the produced 2 : 4-dinitrophenol undergoes no further nitration under the conditions used.

The presence of nitrous acid markedly affects the rate of nitration of *p*-nitrophenol. However, it was found that, over the whole range of these experiments, nitrous acid is neither produced nor destroyed in the course of nitration. No autocatalysis was observed.

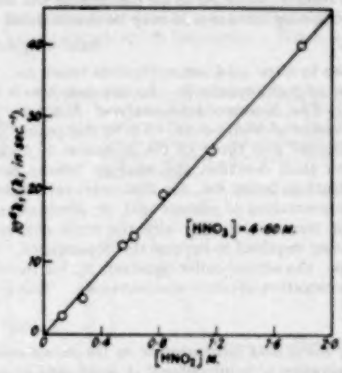
The kinetic results are conveniently presented in two parts, one relating to runs with nitric acid concentrations in the range 1·4—6·0M., a range in which positive catalysis by nitrous acid is dominant, and the other referring to nitric acid concentrations in the range 7·0—10·0M., where negative catalysis by nitrous acid supervenes.

FIG. 12.



General kinetic form of the nitration of p*-nitrophenol in acetic acid by nitric acid in the concentration range* 1·4—6·0M. *in the presence of nitrous acid : illustrated by Run No.* 324. *Temperature* 20·87°. $[HNO_3]$ = 4·60M. $[HNO_2]$ = 0·627M. *Initially* $[NO_2{\cdot}C_6H_4{\cdot}OH]$ = 0·025M. *First-order rate constant,* k_1 = 0·00134 *sec.*$^{-1}$.

FIG. 13.



Dependence on nitrous acid concentration of the first-order rate constants of nitration of p*-nitrophenol by* 4·60M*-nitric acid in acetic acid at* 20·87°.

(6.2) *The Nitrous Acid-catalysed Reaction. Reaction Order with Respect to the Aromatic Compound.*—The course of a typical kinetic run, as observed in nitrations with nitric acid concentrations in the range 1·4—6·0M., is illustrated by the logarithmic plot in Fig. 12. It shows that the run obeys the first-order law very accurately. Throughout the stated range of concentrations of nitric acid, first-order reactions are observed, except when, near the upper end of the range, the concentration of nitrous acid is very small.

The first-order nature of these reactions was confirmed in a few cases by conducting pairs of runs with the same nitration solution, and at the same temperature, but with different initial concentrations of *p*-nitrophenol. In all such pairs of experiments consistent first-order rate constants were obtained, as the following example illustrates :

Common solution : $[HNO_3]$ = 3·0M. ; $[HNO_2]$ = 0·2M. Temp. 19·98°.

No. 311. Initial $[C_6H_5O_3N]$ = 0·0225M. k_1 = 0·00140 sec.$^{-1}$
No. 312. ,, ,, = 0·0450M. k_1 = 0·00138 ,,

(6.3) *The Nitrous Acid-catalysed Reactions (continued). Reaction Order with Respect to Nitrous Acid.*—Blocks of runs were carried out at several nitric acid concentrations within the range 1·4—6·0M., in order to determine how the first-order rate constants vary with the concentration of nitrous acid. The record of a block, one relating to the nitric acid concentration 4·6M., is given in Table VIII.

TABLE VIII.

Nitration of p*-nitrophenol in acetic acid by nitric acid in the concentration range* 1·4—6·0M. *Example showing the dependence of the first-order rate constant* (k_1 *in sec.*$^{-1}$) *on the concentration of nitrous acid.*

Temp. 20·87°. $[HNO_3]$ = 4·60M. Initially $[C_6H_4O_3N]$ = 0·025M.

Run no.	327	323	325	324	329	328	322
$[HNO_2]$	0·135	0·276	0·453	0·627	0·816	1·188	1·787
10^4k_1	2·34	4·87	12·2	13·4	19·5	24·7	39·9

The nature of the result here illustrated will be clear from Fig. 13. It is typical of the nitrations of *p*-nitrophenol in acetic acid by nitric acid, within the range of concentrations now under discussion, that the first-order rate constants are directly proportional to the concentration of nitrous acid. There is no residual rate, or at most a very small one, in the absence of nitrous acid.

The results presented so far concerning the nitration of *p*-nitrophenol by nitric acid in acetic acid containing nitrous acid may be summarised in the equation

$$\text{Rate} = k_3[\text{ArH}][HNO_3]$$

It applies to nitric acid concentrations below 6M. The same kinetic formula was obtained for the nitration of *p*-chloroanisole. In this case also it applied to nitric acid concentrations below 6M.

(6.4) *The Nitrous Acid-catalysed Reaction (continued). Dependence of the Rate on the Concentration of Nitric Acid.*—Up to this point, the analogy between the kinetics of nitration of *p*-nitrophenol and those of the nitration of *p*-chloroanisole holds perfectly. But in the next effect we shall describe, the analogy breaks down. It will be recalled that, for nitric acid concentrations below 6M., the first-order rate constant for the nitration of *p*-chloroanisole with a fixed concentration of nitrous acid, or, alternatively, the second-order constant, k_3, in the above equation, increases steeply with the nitric acid concentration—a sixth-to-seventh power of the latter being required to express the dependence. On the contrary, for nitric acid concentrations below 6M., the second-order constant, k_3, for the nitration of *p*-nitrophenol actually decreases as the concentration of nitric acid increases. This is established by the figures in Table IX.

TABLE IX.

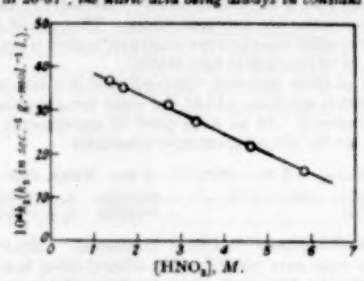
Effect of nitric acid concentration on the second-order rate constants (k_3 *in sec.*$^{-1}$ *g.-mol.*$^{-1}$ *l.*) *for the nitration of* p*-nitrophenol in acetic acid by nitric acid in the presence of nitrous acid.*

Temp. : 20·87°. Initially $[C_6H_4O_3N]$ = 0·025M.

Run no.	$[HNO_3]$	$[HNO_2]$	10^4k_1.	10^4k_3.	Run no.	$[HNO_3]$.	$[HNO_2]$	10^4k_1.	10^4k_3
334	1·38	0·380	13·8	36·3	332	3·35	0·556	15·3	27·5
330	1·68	0·495	17·1	34·9	325	4·60	0·553	12·2	22·0
335	2·70	0·555	17·3	31·2	333	5·83	0·705	11·5	16·3

FIG. 14.

Effect of the concentration of nitric acid on the second-order rate of the nitrous acid-catalysed nitration of p*-nitrophenol in acetic acid at* 20·87°, *the nitric acid being always in constant excess.*



The form of the effect is exhibited in Fig. 14. Over a four-fold increase in the concentration of nitric acid, the second-order rate constant drops linearly to about one-half its initial value.

The form of the relationship appears simple, and the whole effect seems mild, having regard to the usually great sensitivity of nitration rates to nitric acid concentration.

We think that the mild effect results from the approximate cancellation of two opposing strong effects, and that the apparent simplicity is deceptive. There is much evidence that the ability of nitric acid to donate protons, and to produce nitronium ions, and, in suitable circumstances, to produce other active cations, such as nitrosonium ions, increases steeply with the concentration of nitric acid. We must expect, therefore, that the ability of nitric acid to suppress, by proton donation, the last traces of a weak base will increase steeply with the acid concentration. If we assume that the aromatic attack, which leads to nitration, is the attack, say, of a nitrosonium ion on a *p*-nitrophenoxide ion, *i.e.*, of an active cation on a weak base, then the mildness of the effect on rate can be understood as representing the result of an approximate balance between opposing strong effects on the concentrations of the separate reactants.

(6.5) *The Existence of a Nitrous Acid-anticatalysed Reaction*—The kinetics of the nitration of *p*-nitrophenol by nitric acid in acetic acid containing nitrous acid become quite complicated if the nitric acid concentration is above 7M. The closest analogy now seems to be with anisole, rather than with *p*-chloroanisole. Runs with 5M-nitric acid still showed positive catalysis by nitrous acid; but the individual runs were no longer accurately of first-order. When, ignoring

FIG. 15.

Diminished positive catalysis by nitrous acid in the nitration of p*-nitrophenol by* 9·0M*-nitric acid in acetic acid at* 19·97°. *The logarithms of the mean first-order rate constants are plotted against those of the nitrous acid concentrations. The slope of the line is* 0·52.

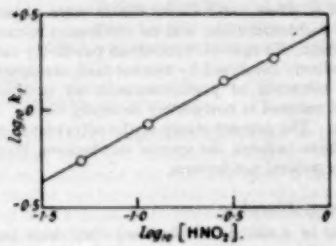
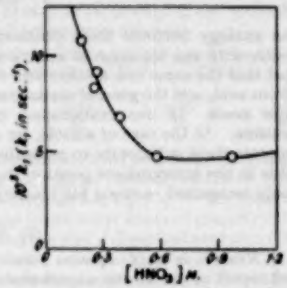


FIG. 16.

Negative catalysis by nitrous acid in the nitration of p*-nitrophenol by* 10·0M*-nitric acid in acetic acid at* 19·97°. *Mean first-order rate constants are plotted against concentrations of nitrous acid.*



the deviations, we calculated mean first-order constants, these constants were found to increase with the nitrous acid concentration much less steeply than corresponds to proportionality. As a rough expression of the connexion, we may say that the rate is proportional to the power 0·5 of the nitrous acid concentration. This is illustrated by the logarithmic plot in Fig. 15. However, the law stated is not exactly obeyed. In particular, the experiments indicate a definite residual rate in the absence of nitrous acid.

When the concentration of the nitric acid is increased to 10M., a substantial negative catalysis by nitrous acid is observed. The runs depart considerably from the first-order form,

TABLE X.

Variation in the rate of nitration of p*-nitrophenol in acetic acid with changes in the concentration of nitric acid at various fixed concentrations of nitrous acid.*

		10^4k_1 at 20·8°.		
[HNO$_3$]		2·0M.	5·0M.	10·0M.
[HNO$_2$]	0·1M.	3·4	2·0	130
	0·5M.	17	10	50
	1·0M.	34	20	50

but are not even approximately of zeroth-order. When we calculate mean first-order constants and plot them against the nitrous acid concentrations, we obtain the curve in Fig. 16. This

shows that negative catalysis enters fairly strongly at the lower nitrous acid concentrations, leaving only a vestigial positive catalysis at the higher concentrations. The experiments indicated a considerable reaction rate in the absence of nitrous acid.

Although the first-order rate constants, for a fixed concentration of nitrous acid, fall as the concentration of nitric acid is increased from 1·4 to 5·8M., the mean, first-order, rate constants rise again as we continue to increase the nitric acid concentration up to 10·0M. The general character of the variation is indicated in Table X, in which the figures relating to 10M-nitric acid must be considered as only approximate. These changes can be understood on the lines already indicated.

Table XI contains, in a summarised form, the main results, described in this Section, concerning the incursion of negative catalysis by nitrous acid in the nitration of *p*-nitrophenol in the higher concentrations of nitric acid in acetic acid. Some results, given in previous Sections, for the positive catalysis of the reaction by nitrous acid in the lower concentrations of nitric acid in acetic acid are similarly summarised for comparison.

TABLE XI.

Summary of the main features of the kinetics of the nitration of p*-nitrophenol by nitric acid in acetic acid containing nitrous acid at 20°.*

Runs no.	$[HNO_2]$	$[HNO_3] = n$.	Type of catalysis by HNO_2.	Rate approx. propl. to :
53—60	2·89	$0·04 < n < 0·25$	+ ve	$a^{1·00}$
322—329	4·60	$0·10 < n < 1·75$	+ ve	$a^{1·00}$
460—469	8·00	$0·04 < n < 0·50$	+ ve	$a^{0·5}$
549—558	10·00	$0·01 < n < 0·50$	− ve	(complicated)
		$0·50 < n < 1·00$	(practically no effect)	

The analogy between these phenomena as a whole, and those which were observed in connexion with the nitration of anisole and of *p*-chloroanisole, will be obvious. It cannot be doubted that the same two mechanisms of nitration, the special mechanism positively catalysed by nitrous acid, and the general mechanism negatively catalysed by nitrous acid, are operative in all three cases. In our examination of the nitration of *p*-chloroanisole we isolated both mechanisms. In the case of anisole, we did not succeed in completely isolating either; but we did separate them sufficiently to recognise them. The present study of the nitration of *p*-nitrophenol is in the intermediate position that we have isolated the special mechanism, though we have only recognised, without fully isolating, the general mechanism.

(7) *Nitration of Phenol.*

(7.1) *Kinetics in Acid–Aqueous Solutions, and in Acetic Acid Solutions.*—We shall make no detailed report of our kinetic experiments on the nitration of phenol, partly for the reason that a number of reports on this complicated subject have already appeared. They relate both to aqueous solvents and to organic solvents (cf. Section 1.2). Catalysis by nitrous acid is the rule; but the power of the nitrous acid concentration to which the nitration rate is proportional is never higher, and is almost always considerably lower, than the first power. Autocatalysis, arising from the production of nitrous acid by oxidation of some of the phenol, has been observed. In water, complex by-products are formed extensively.

The general picture presented by the kinetics of the nitration of phenol in acetic acid has close analogies with that of the nitration of anisole in that solvent (Section 5). It is not difficult to recognise that the same two mechanisms of nitration are in operation. There is catalysis by nitrous acid, which diminishes in intensity with increasing concentration of nitric acid. There is also autocatalysis, and an appreciable formation of complex by-products.

(7.2) *Products in Acid–Aqueous Solutions.*—It has been shown (Bunton, Minkoff, and Reed, *J.*, 1947, 1416) that the mononitration product of phenol consists of *o*- and *p*-nitrophenols only, the proportion of *m*-isomeride constituting less than 0·1% of the mixture. We have made some experiments to determine how the proportions of these products vary with the nitrous acid content of an aqueous acidic nitration medium.

We used strongly acidified aqueous media in these experiments having in mind the possibility of attack on the aromatic nucleus by hydrated forms of the nitronium ion or the nitrosonium ion, *i.e.*, by the nitric acidium ion, $H_2NO_3^+$, or the nitrous acidium ion, $H_2NO_2^+$. Our guide in this part of our work was the series of experiments, described by Halberstadt, Hughes, and Ingold in Part III (*J.*, 1950, 2441), on ordinary aromatic nitration in acidified aqueous media. Here it is

shown that aromatic nitration in aqueous solution depends on the presence of a strong proton-donor.

We employed sulphuric acid as the acidifying acid. The nitration solution also contained salts, since our method of making them up was to dissolve potassium nitrate and potassium nitrite in water, and then add the requisite excess of sulphuric acid. We have assumed that the dissolved potassium hydrogen sulphate made no difference to the proportions of the products.

The results are in Table XII. Errors of several units % are possible in the proportions of the products, especially since the yields of mononitro-products were in the neighbourhood of 70—80% only. However, the change in the product proportions, with the increase of nitrous acid content, is so large that there can be no doubt about its reality.

As to the cause of this effect, we assume that the reagent which attacks the aromatic molecule is different, according to whether nitrous acid is absent (Runs 1, 2), or an excess of nitrous acid is present (Run 5). In view of all we know concerning aromatic nitration in general, and phenolic nitration in particular, it seems an obvious suggestion that, in the absence of nitrous acid, the reagent is either NO_2^+ or $H_2NO_3^+$, whilst, in the presence of excess of nitrous acid, it is either NO^+ or $H_2NO_4^+$. Support for this idea may be derived from the fact that the proportion, 9% : 91%, in which *o*- and *p*-nitrophenols are found in the product of the acid-aqueous mononitration of phenol by nitric acid in the presence of an excess of nitrous acid is exactly the same as the proportion in which Veibel (*loc. cit.*) found *o*- and *p*-nitrosophenols in the product of the acid-aqueous mononitrosation of phenol by nitrous acid in the absence of nitric acid.

The question of whether dehydrated or hydrated cations act is a difficult one. Halberstadt, Hughes, and Ingold, dealing in Part III with general aromatic nitration, attempted to make

TABLE XII.

Effect of nitrous acid on the proportions of o- *and* p-*nitrophenols in the product of the mononitration of phenol by nitric acid in strongly acidified aqueous solutions.*

Temp. : 20°. Initially : [PhOH] = 0·45M. ; [HNO_3] = 0·50M. ; [H_2SO_4] = 1·75M.
($KHSO_4$ was also present in quantity equivalent to the total [HNO_3] + [HNO_2].)

Run no.	1	2	3	4	5
[HNO_2]	0·00	0·00	0·25	0·25	1·00
o-Nitrophenol, %	73	72	55	52	9

plausible the theory that aromatic attack, in highly aqueous acidified solutions, is by the nitric acidium ion, $H_2NO_3^+$. The corresponding conclusion for special phenolic nitration would be that, in such solutions, the effective agent is the nitrous acidium ion, $H_2NO_4^+$. The experiments of this Section can be considered to bear the same relation to the wider study of phenolic nitration reported in this paper, as do the experiments of Part III to the study of general aromatic nitration as reported in Parts I—V of this series.

(7.3) *Products in Acetic Acid Solution.*—We have made some experiments to determine how the proportions, in which *o*- and *p*-nitrophenols occur in the product of the mononitration of phenol by nitric acid in acetic acid, depend on the nitrous acid content of this medium.

We were interested to detect if possible the activity of another conceivable " carrier " of the nitrosonium ion, *viz.*, the dinitrogen tetroxide molecule. Therefore, in the present experiments, we kept the nitric acid concentration in the nitration solutions sufficiently low substantially to exclude nitration by a nitronium ion mechanism. We know (Part II, *J.*, 1950, 2400) that what we here call " nitrous acid " exists in acetic acid mainly in the form of dinitrogen tetroxide. Therefore, we prepared the nitration mixtures by adding known quantities of freshly distilled dinitrogen tetroxide to a solution of nitric acid in acetic acid. This procedure is particularly convenient when large proportions of " nitrous acid " are required.

The main series of results, applying to the temperature 0°, are reported in Table XIII. They are confirmed by two shorter series which were obtained for the temperatures −10° and +20°. The figures can probably be trusted to a few units %. The proportions in which dinitration took place under the conditions used were never more than a few units %, and the proportions in which complex products were formed were comparably small.

Table XIII shows that, so long as the concentration of " nitrous acid," *i.e.*, of dinitrogen tetroxide, remains small in comparison with that of the nitric acid—as it was in all our kinetic experiments—the proportion of *o*-nitrophenol in the mononitrophenols remains fairly constant at about 46% ; but that, as the concentration of dinitrogen tetroxide becomes comparable to that of the nitric acid, the proportion of *o*-nitrophenol increases, rising to more than 70% when the concentration of dinitrogen tetroxide exceeds that of the nitric acid.

TABLE XIII.

Effect of dinitrogen tetroxide on the proportions of o- and p-nitrophenols in the product of mononitration of phenol by nitric acid in acetic acid.

Temp.: 0°. Initially, [PhOH] = 0·6*M*.; [HNO_3] = 3·2*M*.

Run no.	8	9	10	11	12	13	14	15
[N_2O_4]	small	small	0·030	0·27	1·8	3·2	3·5	4·5
o-Nitrophenol, %	44	49	45	46	64	68	70	74

Our main guide in the interpretation of these results is analogy with the work, reported in Part IV (*J.*, 1950, 2452), on ordinary aromatic nitration with dinitrogen pentoxide as the reagent. It was shown that the nitrating properties of this substance differ according to whether, as in the presence of nitric acid, it is ionised to give the nitronium ion, or whether, as in the absence of nitric acid, it remains covalent in an organic solvent. In the former case the free nitronium ion attacks the aromatic compound. In the latter, the dinitrogen pentoxide molecule itself is the attacking reagent, acting as a " carrier " of the nitronium ion into the aromatic molecule.

Goulden and Millen have shown (*J.*, 1950, 2620) that, just as dinitrogen pentoxide is ionised by nitric acid to give the nitronium ion, so dinitrogen tetroxide is ionised in nitric acid to give the nitrosonium ion. But in the absence of nitric acid, or of a sufficient excess of nitric acid, dinitrogen tetroxide remains largely covalent in an organic solvent.

The general view which we shall develop concerning those nitration mechanisms which are especially applicable to the nitrations of phenols and phenolic ethers will involve the conclusion that, in ionising conditions, the entity which attacks the aromatic molecule is the nitrosonium ion, NO^+. This should be the effective reagent when (as in Runs 8—11) the nitric acid is in sufficiently large excess over the dinitrogen tetroxide to secure extensive ionisation of the latter. But when the concentration of dinitrogen tetroxide is large, and when the proportion of nitric acid is insufficient to secure its adequate ionisation (as in Runs 12—15), then we might expect the covalent dinitrogen tetroxide molecule, N_2O_4, itself to become the attacking reagent, acting as a " carrier " of the nitrosonium ion into the aromatic molecule. The fact that the proportions of products alter as they do shows that some significant change of reagent occurs in these circumstances; and the change that we have suggested seems plausible, having regard to the known ionising properties of dinitrogen tetroxide. Thus the experiments of this Section can be considered to bear the same relation to the wider study of phenolic nitration reported in this paper, as do the experiments of Part IV to the study of general aromatic nitration as reported in Parts I—V of this series. Just as we envisage a series of " carriers " of the nitronium ion, *e.g.*, NO_3^+, $H_2NO_3^+$, N_2O_5, NO_2Bz, in order of diminishing activity, so we contemplate a series of possible " carriers " of the nitrosonium ion, *e.g.*, NO^+, $H_2NO_3^+$, N_2O_4, etc.

(8) *Coloured By-products of Nitration, particularly of Anisole.*

We have now described our observations on the mechanisms of ***nitration*** of phenolic ethers and phenols; but there remain for consideration the non-nitrating side reactions. These side reactions are partly non-oxidative, giving coloured, and in some cases polycondensed, compounds. They are also partly oxidative, producing the already discussed kinetic auto-effects.

We have attacked only the more tractable part of this problem, *viz.*, the non-oxidative formation of non-polycondensed by-products. The chief of the encountered examples in which the total formation of by-products may assume large proportions (*e.g.*, 10%) are the nitration of anisole, which gives a coloured binuclear by-product, as well as polycondensed products, and the nitration of phenol, which, as is well known, gives polycondensed products. We have studied particularly the example of anisole. It is only a conjecture that the polycondensations are elaborations of the relatively simple condensation illustrated in the case of anisole.

The formation of coloured by-products during nitration is not peculiar to the nitration of phenolic ethers and phenols. What is peculiar is that the coloured compounds derived from phenolic ethers and phenols exhibit greater stability, and in particular survive nitration conditions better, than do those derived from aromatic hydrocarbons or halogeno-hydrocarbons. Benford and Ingold studied the unstable crimson colours that appear during the nitration of aromatic hydrocarbons and halogeno-hydrocarbons in organic solvents (*J.*, 1938, 947). They showed that the reagents necessary to produce the coloured substances were the aromatic compound, some form of " nitrous acid," and some strong acid, which in nitration conditions was nitric acid, though this could be replaced by other strong acids. The same authors showed that

the coloured compounds were formed reversibly, in equilibrium with their factors; one result of this was that, as the aromatic compounds became consumed in the nitration process, the colours disappeared. Finally, these authors found that, although the equilibrium proportions in which the coloured compounds were produced were small, they tended to increase with the general reactivity of the aromatic compound. Benford made the acute suggestion (Thesis, London, 1938, p. 139) that the coloured substances might be radicals of the diarylaminyl oxide type, Ar_2NO, though he was not able at that time firmly to establish this idea.

During the nitration of anisole in acetic acid in the presence of nitrous acid, a deep purple colour is produced. The colour does not disappear as the anisole becomes consumed in nitration. This coloured substance has been definitely identified as the dianisyloxidoammonium ion, $\{(MeO\cdot C_6H_4)_2NO\}^+$, by a direct comparison of its absorption spectrum with that of the salt, dianisyloxidoammonium perchlorate, prepared from anisole and nitric acid by K. H. Meyer and Gottlieb-Billroth (*Ber.*, 1919, **52**, 1476).

The proportions in which this cation is produced during the nitration of anisole in acetic acid have been measured colorimetrically for a number of different conditions. These proportions may be quite large, and are frequently in the range 5—15%.

The diarylaminyl oxides are odd-electron radicals. But the more basic of them form non-radical salts with loss of an electron. This means that some substance, which may be the substance supplying the anion of the salt, or a portion of the free radical, or some foreign substance, becomes reduced. The salt-forming reaction with elemental bromine can be represented as follows (here the halogen is reduced):

$$R_2NO + \tfrac{1}{2}Br_2 = (R_2NO)^+Br^-$$

The formation of dianisylaminyl oxide from anisole and "nitrous acid," under the influence of an acid condensing agent, can be formally represented as a condensation between anisole and the free-radical nitrogen dioxide:

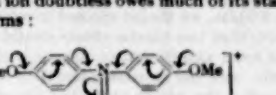
$$2MeO\cdot C_6H_5 + NO_2 = (MeO\cdot C_6H_4)_2NO + H_2O$$

This equation may not be mechanistically correct, but it at least expresses the need for "nitrous acid." Dianisylaminyl oxide is a moderately strongly basic radical; and it is converted by excess of nitric acid into the non-radical salt, dianisyloxidoammonium nitrate. The conversion must involve a reduction of some nitric acid, and therefore a restoration of some "nitrous acid." We can formally represent the restored "nitrous acid" as nitrogen dioxide:

$$(MeO\cdot C_6H_4)_2NO + 2HNO_3 = \{(MeO\cdot C_6H_4)_2NO\}^+NO_3^- + H_2O + NO_2$$

It is then seen, by addition of the last two equations, that the over-all reaction is non-oxidative.

The diaminyloxidoammonium ion doubtless owes much of its stability to a partial mesomeric conversion into oxonium ionic forms:



This is only a modernisation of the quinonoid theory of the structure of the ion, which was originally put forward by Meyer and Gottlieb-Billroth (*loc. cit.*).

(9) *Catalysis by Nitrous Acid outside the Field of Phenol and Aniline Derivatives. Nitration of Mesitylene.*

We have given our results relating to the special mechanism operating in the nitration of derivatives of phenol. We shall show in Part VII that it also operates in the nitration of derivatives of aniline. One further matter required experimental examination. This was the question of why the special mechanism has always appeared to be peculiar to derivatives of phenol and aniline; why it supplants the general mechanism of nitration in these particular cases; and why, if it can do that, it does not take some notable part in aromatic nitration universally.

For a long time we have had a hypothetical answer to this question. It is that, in principle, the special, nitrous acid mechanism *is* universal, just as is the general, nitronium ion mechanism; but that the special mechanism receives special advantages from the use of an aromatic compound of high nuclear reactivity, independently of what particular substituents confer such

reactivity on the nucleus. We think that the special mechanism supplies a reagent—the nitrosonium ion—which is more stable and less reactive than the reagent—the nitronium ion—which is furnished by the general mechanism. If only the general mechanism of nitration existed, we should inevitably have greatly to milden the conditions of nitration, *i.e.*, restrict the nitronium ion supply, whenever we attempted to study the *mono*nitration of such a highly reactive substance as anisole or phenol. Actually, such a reduction in the opportunities for the general mechanism simply leaves the field open for the special mechanism; for this is not necessarily impeded by those changes of conditions which are made for the purpose of repressing the nitronium ion (cf. Millen, *J.*, 1950, 2600). And if only the special mechanism existed, many aromatic compounds would not, or would only with difficulty, be nitrated; for the active reagent is less electrophilic than is that provided by the general mechanism (*idem*, *ibid.*). But the special mechanism is quite adequate to cope with the nitration of such highly reactive nuclei as those present in derivatives of phenol and aniline.

It was clear to us that in order to establish this assumed universality of both mechanisms, two things had to be done. First, we had to show that the general mechanism does not become abrogated in the nitration of derivatives of phenol and aniline, but applies to these as to other aromatic compounds. This has been done for derivatives of phenol, inasmuch as we show (Sections 3.4, 3.5, 5, 6.5, and 7.1) that the much-discussed complications applying to the nitration of phenolic ethers and phenols arise, not from the suppression of the general mechanism of nitration, but from the adding to it of the special mechanism (and the adding also, in some cases, of non-nitrating side reactions). Our second task was the complement of this: we had to show that the special mechanism of nitration was not peculiar to derivatives of phenol and aniline, but could be observed outside that field, for instance, in the nitration of a hydrocarbon. That is the theme of the work now to be reported.

According to our view of the facility of occurrence of the two nitration mechanisms, an aromatic hydrocarbon of high nuclear reactivity should offer a comparatively good chance for an observation of the incursion of the special mechanism of nitration. Therefore, we selected for this study one of the more reactive of the aromatic compounds previously investigated by us, namely, mesitylene.

The nitration of mesitylene by the general, nitronium ion mechanism in acetic acid as solvent has been described in Part II (*J.*, 1950, 2400). With nitric acid in constant excess, the reaction seems to be weakly anticatalysed by nitrous acid. The conditions in which these statements have been illustrated are relevant to the comparison now to be made. They are as follows: temperature, 20°; $[HNO_3]$, 5—7M.; $[HNO_2]$, below 0·014M.

Now we have seen that the special, nitrous acid mechanism, when in isolation, produces a reaction which is of first order with respect to the aromatic compound, and of first order with respect to nitrous acid. It follows that, if, by increasing the nitrous acid content of the nitration solutions considerably above 0·014M., we should succeed in realising a substantial incursion of the special mechanism of nitration, then two kinetic effects should be observed. First, the absolute rates, with all concentrations fixed except that of nitrous acid, should increase with increasing concentration of nitrous acid; and the increase should be approximately linear, or at least asymptotically linear. Secondly, the zeroth-order law should break down, giving place, at first, to a mixed, zeroth-to-first order kinetic form, and eventually, if the special mechanism can be made sufficiently dominating, to an approximate first-order form.

TABLE XIV.

Dependence of the initial nitration rate of mesitylene in acetic acid at 25·0° on the concentration of nitrous acid.

Initially, $[HNO_3] = 5{\cdot}7$M., $[C_6H_3Me_3] = 0{\cdot}08$M. (the same throughout).

Run no.	586	587	585	584	583
$[HNO_2]$, M.	0·018	0·055	0·084	0·210	0·317
$-dA/dt$ in mm. $sec.^{-1}$	0·0033	0·0040	0·0046	0·0070	0·0088

A dilatometric study of the influence of nitrous acid on the kinetics of nitration of mesitylene has been made, and both the expected effects have been observed. A convenient way of comparing absolute rates at standardised concentrations is to measure initial rates in runs conducted under standardised initial conditions. Such a set of initial rates, obtained for a block of runs in which all initial concentrations were the same, except the concentration of nitrous acid, is given in Table XIV. It will be noticed that the lowest of the nitrous acid concentrations, 0·018M., is

higher than the upper limit of those used in the above-mentioned experiments recorded in Part II; and that, in the present block of runs, the concentration of nitrous acid is increased to more than 20 times that limit. One sees that the rates increase considerably with increasing concentration of nitrous acid. The form of the increase is simple, as is shown in Fig. 17.

From this result it is clear that we are observing, superposed on a reaction which does not require nitrous acid, and is evidently the nitronium ion reaction, a second reaction, the rate of which is proportional to the concentration of nitrous acid. Thus we identify one of the two main kinetic criteria of the nitrous acid mechanism.

FIG. 17.

Initial rates of nitration (expressed as rates of fall of height in the same dilatometer) of mesitylene (in the same initial concentration, about 0·08M.), by 5·7M-nitric acid in acetic acid at 25°, are plotted against the concentrations of nitrous acid. The linear curve shows that a reaction catalysed by nitrous acid is present, as well as a reaction which does not depend on nitrous acid.

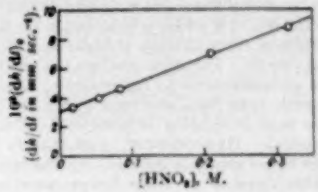
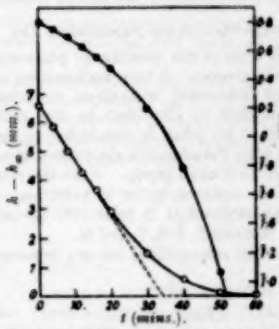
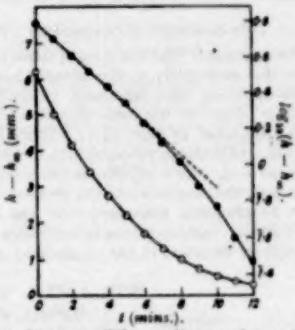


FIG. 18.



Run no. 586: ordinary plot and logarithmic plot of the course of the nitration of mesitylene by 5·71M-nitric acid in acetic acid at 25·0° in the presence of 0·018M-nitrous acid.

FIG. 19.



Run no. 580: ordinary plot and logarithmic plot of the course of the nitration of mesitylene by 5·71M-nitric acid in acetic acid at 30·0° in the presence of 0·56M-nitrous acid.

It will be clear from Fig. 17 that we can scarcely expect to isolate the nitrous acid mechanism in a pure form, and thus to observe a pure first-order reaction with respect to the mesitylene, within the permissible range of concentrations of nitrous acid. (The concentration of nitrous acid has always to be low in comparison with the concentration of nitric acid: otherwise the "nitrous acid" would not retain the same properties—see Section 7.3.) With 0·3M-nitrous acid the special mechanism is about twice as important as the general one. Overall in these experiments, we have used concentrations of nitrous acid up to 0·6M., which seemed about as far as it was wise to go. However, this suffices to give a considerable degree of domination to the nitrous acid mechanism, and therefore it allows us to observe a moderately close approach to first-order kinetics, though not a pure first-order reaction.

Figs. 18 and 19 will establish that the reaction order with respect to mesitylene does indeed rise from a little above zero to a little below unity over the range of nitrous acid concentrations stated. Each figure shows, for the kinetic run to which it refers, both a plot of the variable part of the dilatometric height, and a plot of its logarithm, each against time. Fig. 18 relates to a run in which the concentration of nitrous acid was only 0·018M. One sees that about the first half of the reaction proceeds at a practically constant rate, whilst the logarithmic plot is curved throughout its length. Evidently the reaction order is here approximating to zeroth order. Fig. 19 refers to a run in which the concentration of nitrous acid was 0·56M. In this case the whole of the reaction–time graph is curved, whilst a considerable portion of the reaction yields a linear logarithmic plot. Obviously this reaction is approaching a first-order form. Thus we recognise in our results the second of the two main kinetic characteristics of the nitrous acid mechanism.

As the first kinetic property by which we recognise the special mechanism is the acceleration of nitration by nitrous acid, it was necessary to prove that this did not arise from the simultaneous incursion of a form of side-chain nitration induced by nitrous acid. And as the recognition of the second characteristic, *viz.*, the increased kinetic order, depends on the observation, not of initial rates, but of the general course of the reaction, it was necessary to show that the relatively lower rate in the later part of the reaction, which is observed in the presence of much nitrous acid, does not result from the incursion of a second stage of nitration. Both these points were covered in the course of our chemical checks. The main product obtained in preparative experiments carried out under conditions comparable as to temperature, time, and the concentrations of reagents with those of the kinetic runs, including runs with a low (*e.g.* 0·01M.) and with a high (*e.g.*, 0·3M.) content of nitrous acid, in solution of nitric acid (5·7M.) in acetic acid, was always the nuclear mononitration product. Its accelerated production in presence of nitrous acid was qualitatively confirmed by the larger amounts isolated, and the smaller quantities of mesitylene recovered (after equal nitration times at the same temperature) in the presence, than in the absence, of much nitrous acid. As far as could be ascertained, no substantial amount of side-chain nitration, or of dinitration, took place under the conditions of the kinetic experiments.

(10) *Summary of Conclusions* : *Nitration through the Nitrosonium Ion.*

We have concluded that the complexities which arise in the nitration of phenolic ethers and phenols are due essentially to the simultaneous effectiveness of two mechanisms of nitration, though non-nitrating side reactions, oxidative or otherwise, sometimes contribute further complications. One of the two nitration mechanisms is identified as the nitronium ion mechanism elucidated in Part II (*J.*, 1950, 2400). The other is concluded to be a similar mechanism in which the nitrosonium ion combines with the aromatic electrons : thus a nitroso-group is introduced, which rapidly becomes oxidised to a nitro-group. Both the nitronium ion mechanism and the nitrosonium ion mechanism are assumed to be in principle of universal application to aromatic nitration; but the latter mechanism is relatively favoured in the nitration of highly reactive aromatic molecules (cf. Sections 3, 5, 6, 7, and 9).

The equilibria involved in the production of the free nitrosonium ion are presumed to be as follows :

$$HNO_2 + HNO_3 \rightleftharpoons H_2NO_3^+ + NO_3^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$H_2NO_3^+ \rightleftharpoons NO^+ + H_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$NO^+ + NO_3^- \rightleftharpoons N_2O_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Equations (1) and (2), which show the nitrous acidium ion as an intermediate, are hypothetical, but are supported by analogy with the well-established equilibria leading to the nitric acidium ion, and thence to the nitronium ion (cf. Part II, Section 2.4.1, *J.*, 1950, 2419). Equation (3) has to be added because dinitrogen tetroxide is a weak electrolyte in solutions of nitric acid in organic solvents, whereas the corresponding ionic equilibrium involving dinitrogen pentoxide could be neglected in the considerations of Part II concerning the production of the nitronium ion because dinitrogen pentoxide is a strong electrolyte in such solutions (cf. Part II, Section 4.2.1, *J.*, 1950, 2419 ; Goulden and Millen, *J.*, 1950, 2620 ; Millen and Reed, forthcoming papers).

No doubt the free nitrosonium ion is a more effective substituting group than any covalent structure (" carrier ") from which it can be liberated on interaction with the aromatic nucleus. But we have tried to make plausible the view that, just as the nitronium ion may be carried into reaction in combined forms, such as $H_2NO_3^+$, N_2O_5, and NO_2Br (Parts III, IV, and V, *J.*, 1950, 2441, 2452, 2467), so also the nitrosonium ion can in forms such as $H_2NO_3^+$ and N_2O_4, and perhaps N_2O_3 and NOCl (Sections 7.2 and 7.3).

The simplest view that can be taken of the reaction of the nitrosonium ion with the aromatic nucleus applies when no point of attachment for the ion is presented by any side chain. We assume that a rate-determining addition of the nitrosonium ion is succeeded by a fast ejection of the aromatic proton, and a fast oxidation of the nitroso-compound to a nitro-compound :

$$ArH + NO^+ \xrightarrow[\text{slow}]{} ArHNO^+ \quad . . . . . (4)$$

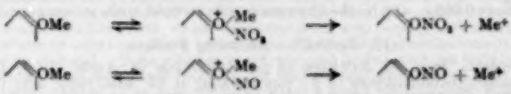
$$ArHNO^+ \xrightarrow[\text{fast}]{} ArNO + H^+ \quad . . . . . (5)$$

$$ArNO + HNO_3 \xrightarrow[\text{fast}]{} ArNO_2 + HNO_2 \quad . . . . . (6)$$

Reactions (4) and (5) are assumed, and are supported by analogy with the proved course of nitronium ion nitration (Part II, Section 3.2, *J.*, 1950, 2426). Reaction (6) has necessarily to be assumed in order to account for the stoicheiometry of the process.

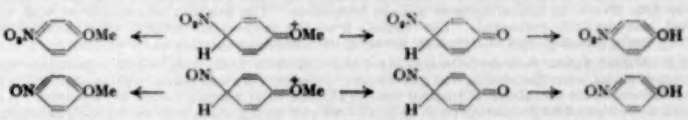
Having recognised the general character of the mechanisms operating in the nitration of phenols and phenolic ethers,* we shall endeavour to secure direct kinetic evidence for those detailed steps in the special mechanism, which at present rest only on arguments of analogy (*viz.*, those of equations 1, 2, 4, and 5).

The nitration of phenolic ethers and phenols presents the complication that there is, in the side chains of these molecules, a point of attachment for a reactive cation, be it a nitronium ion or a nitrosonium ion. A possible chemical consequence of this is recognised in the observation that phenolic ethers are partly dealkylated during nitration, by either the nitronium ion mechanism or the nitrosonium ion mechanism (Section 2.1). The assumed dealkylation mechanisms may be illustrated for demethylation as follows :



The aryl nitrate, or nitrite, will undergo rapid acidolysis, and will be isolated as a phenol. The methyl cation will combine with the most accessible anion, *e.g.*, an acetate ion if the solvent is acetic acid.

A second possibility was suggested to us independently by Professor J. F. Bunnett and by Professor J. W. Cook, whom we thank for permission to quote their ideas. These are that the slow stage of nitration (as in equation 4, or in the analogous equation of the nitronium-ion reaction) leads to an almost fully quinonoid oxonium ion, and that then the proton loss (as in equation 5), and the loss of a methyl cation, have comparable (fast) rates :



We offer three arguments which support either of these suggestions. First, there is evidence (Section 2.1) that the proportion of dealkylation under a single nitration mechanism is independent of the absolute rate of nitration ; this indicates that the processes of dealkylation and of normal nitration have kinetics of the same form. Secondly, dealkylation during nitration is suppressed (Section 4) in 2 : 6-dichloro- and 2 : 6-dimethyl-anisole ; this suggests steric hindrance in the formation, either of a branched side-chain, as in the first of the postulated mechanisms, or of the fully quinonoid structure (with the methyl group sideways to the oxygen double bond, and fixed in the plane of the ring), as in the second. Thirdly, the methyl group eliminated during the nitration of *p*-chloroanisole in acetic acid as solvent has been recovered as methyl acetate ; this makes it practically certain that the group is indeed eliminated as a methyl cation (Section 2.2).

We need not deal further with effects due to ion-formation by proton transfer in phenol derivatives; for the theory of such effects in aromatic substitution is today a commonplace.

* In an earlier report (*Nature*, 1946, **158**, 514), we intimated that we were inclined to follow Veibel in assuming the intermediate formation of reactive addition compounds between derivatives of phenol and nitrous acid ; we no longer consider that assumption necessary.

However, the effects may be chemically very significant, as has been illustrated in the example of *p*-nitrophenol, which almost certainly nitrates largely through its anion (Section 4.6).

Finally, as to non-nitrating side reactions, we have identified the principal one which anisole undergoes in our conditions: it involves condensation of the anisole with nitrous acid (or a lower oxide of nitrogen), and produces the coloured dianisyloxidoammonium cation, derived from the radical dianisylaminyl oxide. This makes it probable that the unstable coloured products, which commonly appear (Part I, *J.*, 1938, 947) during the nitration of aromatic compounds with nitric acid containing nitrous acid, are derivatives of diphenylaminyl oxide, as Benford first suggested (Section 8).

(11) *General Experimental Methods.*

(11.1) *Materials.*—Nitric acid, acetic acid, and dinitrogen tetroxide were purified as noted in Part II (*J.*, 1950, 2400). When nitrating solutions containing considerable concentrations of so-called nitrous acid were required, the "nitrous acid" was added in the form of freshly distilled dinitrogen tetroxide. Solutions containing small concentrations of nitrous acid were usually made by mixing solutions free from nitrous acid with solutions relatively rich in nitrous acid. The various phenols and phenol ethers were prepared or purified by well-known methods.

(11.2) *Kinetics.*—Tapless dilatometers, essentially of Benford and Ingold's "type C," were again employed. The use of such dilatometers with a detachable upper bent portion, as described in Part II (*loc. cit.*), was developed in the course of the work. The significance of dilatometric indications was frequently checked by chemical analysis, usually at the ends of the runs, but sometimes also throughout the course of a run, as illustrated in Section 3.2.

(11.3) *Analysis.*—Organic nitro-compounds in isolated, or in solvent-extracted, samples were determined by titration with titanous chloride in a sodium citrate buffer, the excess of reducing agent being back-titrated with ferric alum. The latter was used to standardise the titanous chloride, and the whole process was standardised by application to pure *p*-nitroaniline. Nitrous acid in the nitration solutions at the beginning and the end of kinetic runs was determined by the chloramine-T method, when in concentration above 0·005M., and by the absorptiometric method, when in lower concentration (cf. Part II, *loc. cit.*).

(12) *Particulars concerning Products.*

(12.1) *Nitro-products from the Nitration of* p-*Chloroanisole in Acetic Acid.*—In a preliminary qualitative experiment, *p*-chloroanisole (5 g.) was nitrated at 25° with nitric acid (15 g.) containing nitrous acid, in acetic acid (50 c.c.) as solvent. After 24 hours, the solution was cooled at 0°. The yellow crystals were collected, crystallised from methyl alcohol, and identified as 4-chloro-2-nitroanisole by their m. p., 96°, and by mixed m. p. with a sample prepared by methylation of 4-chloro-2-nitrophenol (Found: C, 45·0; H, 3·4. Calc.: C, 44·8; H, 3·2%). The remaining acetic acid solution was added to excess of 2N-aqueous sodium hydroxide, and the deep-red precipitate was collected and washed with ether. The filtrate was extracted with ether. The precipitate and the residual aqueous solution were then recombined, acidified, and extracted with benzene. The product derived from this extract was identified as 4-chloro-2 : 6-dinitrophenol by its m. p., 80°, and by mixed m. p. with a sample prepared by nitration of *p*-chlorophenol (Found: C, 32·9; H, 1·3. Calc.: C, 33·0; H, 1·4%).

In quantitative determinations of these two products, amounts of about 1 g. of *p*-chloroanisole were nitrated in solutions made up to 25 c.c., and portions of 5 c.c. were withdrawn for analysis. Each sample was run into 50 c.c. of dilute aqueous sodium hydroxide. The solution was extracted with benzene, acidified, and similarly extracted. The residues from the evaporated extracts were each taken up in 10 c.c. of methyl alcohol, and analysed by titration with titanous chloride as noted above.

(12.2) *Methyl Acetate from the Nitration of* p-*Chloroanisole in Acetic Acid.*—This experiment was done a number of times, with like results, and, on the final occasion, care was taken to prove that the originally taken *p*-chloroanisole contained no trace of methyl alcohol, or of a methyl ester, as impurity. A sample prepared from crystalline *p*-chlorophenol, m. p. 42—43°, by methylation with methyl sulphate and alkali, was fractionated through a 1-metre column packed with glass helices. The *p*-chloroanisole had b. p. 198·2—198·4°/765 mm. (Found: C, 59·3; H, 5·2; Cl, 24·4. Calc.: C, 59·0; H, 5·0; Cl, 24·9%). The acetic acid, similarly fractionated, after the usual pre-treatment at its b. p. with chromic oxide, had m. p. 16·55°. The nitric acid was absolute material, prepared as usual by non-ebullient distillation from sulphuric acid at a low pressure and temperature. When used, it contained a small concentration of nitrous acid.

A mixture of *p*-chloroanisole (36·5 g.), nitric acid (63 g.), and acetic acid (200 c.c.) was kept at 35° for 24 hours. It was then cooled, treated with powdered anhydrous sodium acetate (65 g.), and warmed again to 33—35° while connected to the vacuum line through a series of traps cooled at 0° and −80°. The mixture was allowed to boil briskly under the reduced pressure, and the first 100 c.c. of distillate were fractionated through a vacuum-jacketed micro-column of Vigreux type to yield 2·8 g. of methyl acetate, b. p. 56·0—57·0° (Found: C, 47·6; H, 8·4. Calc.: C, 48·6; H, 8·1%). A determination of the saponification equivalent-weight gave the value 75·1 (Calc.: 74), whilst from an authentic sample of methyl acetate the figures 74·1, 75·5 were obtained; this slight inconsistency was attributed to evaporation during transfer. The material from the nitration had n_D^{24} 1·3619, and the authentic sample also had n_D^{24} 1·3619.

The residue from the distillation under reduced pressure was made alkaline with sodium hydroxide, made up to about 3 l. with water, shaken with 0·5 l. of benzene, and filtered. The solid material was washed with benzene, and the combined benzene extracts were washed with water until the washings were colourless, dried ($CaCl_2$), and distilled. The residue was crude 4-chloro-2-nitroanisole, m. p.

94·5—95·5° (30·8 g., *i.e.*, 66 mols. %). After crystallisation from aqueous alcohol, it had m. p. 96·0—96·5° (Found: C, 45·3; H, 3·3; N, 7·5; Cl, 18·9. Calc.: C, 44·8; H, 3·2; N, 7·5; Cl, 18·9%). The solid residue and aqueous liquors were combined, acidified with concentrated hydrochloric acid, and extracted with benzene. In this way 4-chloro-2 : 6-dinitrophenol in a yield of 14·0 g. was recovered, *i.e.*, 25 mols. %. After crystallisation from light petroleum, it had m. p. 79° (Found: C, 32·9; H, 1·3; N, 13·3. Calc.: C, 33·0; H, 1·4; N, 12·8%). The recovered pure methyl acetate (2·8 g.) is equivalent to 15 mols. %, and therefore accounts for 60% of the weight of methyl group eliminated during the formation of the aromatic demethylation product.

(12.3) *Products of Nitration of* 2 : 6-*Disubstituted Anisoles in Acetic Acid.*—2 : 6-Dichloroanisole was allowed to be nitrated during 7 days at 20° in a 4M-solution of nitric acid in acetic acid, which was about 0·2M. with respect to nitrous acid. The solution was slowly poured into excess of aqueous sodium hydroxide at 0°, and the crystalline precipitate was collected, washed with water, dried, and weighed. It represented a 94% yield of almost pure 2 : 6-dichloro-4-nitroanisole. Crystallised from methyl alcohol, this substance had m. p. 97°. It was identified by mixed m. p. with an authentic specimen.

In contrast to the nitration of *p*-chloroanisole, very little demethylation accompanied the nitration of 2 : 6-dichloroanisole. The formation of free nitrophenols could be observed qualitatively as a red colour in alkaline solution, but the quantity of nitrophenols produced was too small for isolation under our conditions. In contrast to the nitration of anisole in particular, no purple colour appeared during the nitration of 2 : 6-dichloroanisole.

2 : 6-Dimethylanisole (2-methoxy-*m*-xylene) was nitrated under the conditions described above, except that, since the reaction was relatively rapid, only 3 hours were allowed. The neutral product, isolated in the same way, constituted a 96% yield of 4-nitro-2 : 6-dimethylanisole (5-nitro-2-methoxy-*m*-xylene). Crystallised from methyl alcohol, it had m. p. 92°, which was not depressed by admixture with an authentic specimen.

Again a trace, but no more than a trace, of free nitrophenols was produced, as was qualitatively observed by the red colour which was formed in alkaline solution. No purple colour was produced during the nitration of the anisole derivative.

(12.4) *Nitro-products from the Nitration of Anisole in Acetic Acid.*—Anisole was nitrated at 20° in 5M-nitric acid in an acetic acid solution, which was about 0·1M. with respect to nitrous acid. The solution was poured into excess of aqueous sodium hydroxide. The aqueous solution was extracted with ether, acidified, and again extracted. Both ether extracts were red-brown, and the residual aqueous solution was red. Most of the neutral product could be distilled without decomposition at 123—128°/3 mm.; but there was a tarry residue. The acid extract yielded a small amount of 2 : 4-dinitrophenol mixed with an acid tar. As to quantities, the distilled neutral product, consisting of mononitroanisoles (Found: C, 54·6; H, 4·7; NO_2, by titanous chloride, 29·9. Calc.: C, 54·9; H, 4·6; NO_2, 30·1%), constituted a 75% yield. The neutral tar amounted to 10% of the weight of the employed anisole, and the 2 : 4-dinitrophenol and acid tar taken together to about 3% of the weight of the anisole. Thus, more than 12% of material was not recovered, but it will be shown in Section 12.5 that amounts of this order can be accounted for as dianisyloxidoammonium salts.

In a nitration at 20° with 7M-nitric acid in an acetic acid solution, which was about 0·2M. with respect to nitrous acid, much less neutral tar was formed. The yield of mononitroanisoles (Found: C, 54·5; H, 4·6; NO_2, by titanous chloride, 30·0%) was 83%. The neutral tar amounted to about 1%, and the 2 : 4-dinitrophenol and acid tar taken together to about 3%, of the weight of the original anisole. More than 13% of material was not recovered, but, as is shown below, this probably consisted of dianisyloxidoammonium salts.

(12.5) *Formation of Dianisyloxidoammonium Salts in the Nitration of Anisole in Acetic Acid.*—When the purple solution, obtained by nitrating anisole by nitric acid in acetic acid containing nitrous acid, was diluted with ice-cold water, filtered, and extracted with ether, much of the purple colour passed into the ether. This colour was changed to red-brown on drying the ether with sodium sulphate; but the purple colour was restored by passing dry hydrogen chloride into the solution. Purple crystals, believed to consist of dianisyloxidoammonium chloride, were obtained; and the corresponding perchlorate was precipitated by the use of concentrated aqueous perchloric acid. This salt was identified with Meyer and Gottlieb-Billroth's salt, prepared as they describe (*loc. cit.*), by a direct comparison of their properties, and in particular of their optical absorption in the visible region of the spectrum.

A Hilger visual spectrophotometer was used. Samples of perchlorate were prepared for optical measurements by dissolving them in a 4M-solution of hydrogen chloride in acetic acid. The main absorption band has its maximum of intensity at 5750 A. The general form of the band is indicated by the following measurements of optical density (d):

λ, A.	5000	5200	5400	5600	5700	5800	5900	6000	6200	6400
d	0·22	0·19	0·22	0·29	0·32	0·32	0·27	0·20	0·11	0·08

The wave-length of the absorption maximum being used, the spectrophotometer was calibrated for the measurement of concentration of dianisyloxidoammonium ion. Solutions containing different weighed amounts of the perchlorate were made up in acetic acid containing hydrogen chloride, and the optical densities were measured in a 1-mm. cell. An approximately linear relationship between concentration and optical density was obtained, as is illustrated by the following figures (the concentrations, c, are in 10^{-4} g./c.c.):

c	58	114	240	750	1110	1600
d	3·2	12·0	21·3	68·0	109	176

These data were used in order to estimate the amounts of dianisyloxidoammonium salts, which were formed during the nitration of anisole by nitric acid containing nitrous acid in acetic acid under various conditions. The proportions in which anisole was converted into the coloured cation during nitration were observed to vary from less than 1% to more than 20%, depending on the conditions.

For nitric acid concentrations in the range 3—7M., and nitrous acid concentrations in the range 0·01—0·50M., the proportion of anisole converted into the coloured ion during nitration, with fixed concentrations of nitric and nitrous acids, was found to be nearly independent of the initial concentration of anisole. This is an indication that nitration, and the condensation leading to the coloured cation, are reactions of the same order with respect to the anisole. The result is illustrated, for two blocks of runs, by the figures in Table XIV.

TABLE XIV.

Proportion of dianisyloxidoammonium ion formed during the nitration of anisole by nitric acid containing nitrous acid in acetic acid at 20°.

	$[HNO_3] = 3M.$		$[HNO_3] = 0·0125M.$		$[HNO_3] = 7M.$	$[HNO_3] = 0·100M.$	
Run no.	607	608	609	610	615	616	617
Initial [PhOMe] ...	0·027	0·054	0·073	0·107	0·026	0·055	0·078
% Ion formed ...	23·4	22·6	24·2	27·8	4·8	5·8	6·9

(12.6) *Nitro-products from the Nitration of Phenol in Water and in Acetic Acid.*—The nitration solutions were poured into an excess of cold dilute aqueous sodium hydroxide, and the alkaline solutions were first shaken with salicylic acid until no more of the latter would dissolve, and then extracted with *iso*butyl acetate. This procedure produced solutions which contained all the formed *o*- and *p*-nitrophenols but were almost entirely free from 2 : 4-dinitrophenol, often simultaneously produced in small amount. The nitrophenols were collected from the ester solution by extraction with 4N-aqueous sodium hydroxide, and this aqueous solution was acidified, filtered from salicylic acid, and extracted three times with one-tenth of its volume of carbon tetrachloride. The *p*-nitrophenol remaining in the aqueous solution was then determined by titration with titanous chloride in a sodium citrate buffer. The *o*-nitrophenol extracted by the carbon tetrachloride was passed back into an alkaline aqueous solution, which was then neutralised, and similarly analysed by titration with titanous chloride.

This method of estimating the proportions in which *o*- and *p*-nitrophenols are present in the mononitration product of phenol gives values for the proportion of *o*-nitrophenol, which are too large when the actual proportion of *o*-nitrophenol is small. Deviations of this type can be calculated from recorded solubility and partition data; but the observed deviations were greater than those calculated, and the necessary corrections were therefore empirically evaluated. They are as follows:

Observed *o*-nitrophenol (%)	20	40	53	63	70	75
Subtract (%)	6	5	4	3	2	1

These corrections have already been applied to the results recorded in Sections 7.2 and 7.3.

(12.7) *Products of Nitration of p-Nitrophenol in Acetic Acid.*—Routine chemical checks, under conditions comparable to those of the dilatometrically followed nitrations described in Section 6, showed that 2 : 4-dinitrophenol was substantially the sole nitration product. It was identified by m. p. and mixed m. p. with genuine material.

(12.8) *Products of Nitration of Mesitylene in Acetic Acid.*—Preparative experiments were carried out under conditions comparable with those of the kinetic runs reported in Section 9. The only change made was to use mesitylene in 0·3M-concentration, instead of 0·1M., in order to provide more material for isolation, and, correspondingly, to employ 5·8M-nitric acid, instead of 5·7M, in order that the average concentration over the course of the run would be the same as before. Proportions of nitrous acid, temperatures, and times were as for the kinetic runs. The products were poured into aqueous sodium hydroxide, and steam-distilled, and the residues were extracted with ether, acidified, and again steam-distilled, and extracted with ether. The general nature of the results has been indicated in Section 9. The bulk of the product appeared in the first steam-distillate; it consisted of a mixture of unchanged mesitylene, together with the main product, nuclear mononitromesitylene. The proportions varied, *inter alia*, with the nitrous acid content of the nitration solution. Thus, after 30 minutes at 25°, only about 50—60% of the mesitylene was nitrated in the presence of 0·01M-nitrous acid, whilst 80—90% was nitrated in the presence of 0·3M-nitrous acid (added as dinitrogen tetroxide). The mesitylene and nitromesitylene were separated by distillation, and the latter substance, distilled samples of which had m. p.s about 40°, and, after crystallisation from methyl alcohol, 42—43°, was identified by mixed m. p. with a genuine specimen. Small amounts of impure alkali-soluble nitro-compound were obtained by extraction with ether from the second steam-distillate; and the residues from the two steam-distillations, on extraction with ether, yielded traces of an impure solid which was acidic, and small amounts of a gummy neutral material. It appeared that, although the nuclear mononitration is accompanied by side reactions, the amounts of the by-products are only of the order of 1%—too little to have any bearing on the interpretation of the kinetic results.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1.

[*Received, December 17th*, 1949.]

513. *Kinetics and Mechanism of Aromatic Nitration. Part VII. Products of Nitration of Aniline Derivatives, especially of Dimethylaniline. The Concomitant Dealkylation of Dialkylanilines.*

By J. Glazer, E. D. Hughes, C. K. Ingold, A. T. James, G. T. Jones, and E. Roberts.

The successive stages involved in the nitration, and concomitant demethylation, of dimethylaniline, finally to give *N* : 2 : 4 : 6-tetranitromethylaniline, are analysed; and consideration is given to the question of how far the various steps require nitrous acid, or proceed independently of nitrous acid.

In strongly acid conditions dimethylaniline is nitrated, presumably through its conjugate acid, with nitronium ion as the reagent, to give the *m*-nitro-derivative. At lower acidities, nitration through the free base ensues, to yield the *o*- and *p*-nitro-compounds, in the ratio of about 1 : 2, and then the 2 : 4-dinitro-derivative. The rates of the stages, parent ⟶ *p*-nitro- ⟶ 2 : 4-dinitro-, are of the same order of magnitude, possibly because the smaller proportion in which free base is present in the nitration of the parent off-sets the deactivating effect of the nitro-group in the *p*-nitro-derivative. In the reaction route, parent ⟶ *o*-nitro- ⟶ 2 : 4-dinitro-, the second stage is much slower than the first. This is attributed to a steric interference by the *o*-nitro-group of nuclear activation by the dimethylamino-group. These nitration stages are highly dependent on nitrous acid when the availability of the nitronium ion is low, but are notably less so when it is high.

Six intermediates are encountered on the nitration routes from 2 : 4-dinitrodimethylaniline to *N* : 2 : 4 : 6-tetranitromethylaniline: they are 2 : 4-dinitromethylaniline, and its *N*-nitroso- and *N*-nitro-derivatives, 2 : 4 : 6-trinitrodimethylaniline, and 2 : 4 : 6-trinitromethylaniline, and its *N*-nitroso-derivative. Different routes through these intermediates are followed in different circumstances. In nitration by 40—70 vol. % aqueous nitric acid, or by nitric acid in *ca.* 50 vol. % aqueous sulphuric acid, a primary demethylation to the secondary amine is followed by *N*-nitrosation, then by *C*-nitration, and then by the final modification of the side chain. In nitration by 70—100 vol. % aqueous nitric acid, or by nitric acid in *ca.* 70 vol. % aqueous sulphuric acid, the primary dealkylation is succeeded by *N*-nitration, then by intramolecular transference of the *N*-nitro-group to the nucleus, and finally by re-nitration in the side chain. In nitration by nitric acid in 95 vol. % aqueous sulphuric acid, the primary reaction is nuclear nitration, and the side chain is only subsequently demethylated and nitrated. The primary demethylations always depend on nitrous acid. *N*-Nitrations apparently utilise the nitric acidium or the nitronium ion, but not the nitrosonium ion. The primary nuclear nitration is not assisted by nitrous acid; unlike the entry of the first and the second nuclear nitro-group into dimethylaniline which can apparently be effected through some form of nitrosonium ion, the direct introduction of the third nuclear nitro-group definitely requires intervention of the nitronium ion.

The mechanism of dealkylation of aromatic tertiary amines during nitration has been further considered. The essential reagent is nitrous acid in some form. Only one alkyl group is eliminated. The reaction is oxidative, the earliest isolable form of the eliminated group being the aldehyde. But the order of ease of elimination of different alkyl groups (*e.g.*, methyl > benzyl) is not the normal order of ease of oxidation. Although the aromatic product is often isolated as the nitrosamine, the steps in the formation of this product can be separated by the use of a weakly polar solvent; and it has thus been shown that the earliest isolable product is the secondary amine. Quite different phenomena appear when alkyl groups are removed from an aromatic tertiary amine by ordinary oxidising agents, such as chromic or permanganic acids: for then two alkyl groups can be successively eliminated to give first a secondary and finally a primary amine; and different alkyl groups are removed in the normal order of ease of oxidation.

All these points are covered by a theory which regards the dealkylation by nitrous acid as a homolytic nitrogen-oxidation, and as dependent in its mechanism on the considerable stability of both NO^+ and NO; the former is assumed to add to the unshared electrons, and the latter to split off, removing one electron from the nitrogen atom, and leading to a loss of an alkyl group after rearrangement.

From the preceding paper and this one, it follows that the dealkylation of phenolic ethers, or of tertiary aromatic amines, by nitrous acid may pursue heterolytic and homolytic mechanisms. Both are in principle universally available. Both commence with the formation of nitrosoxonium or nitrosammonium ions. The dealkylation will be heterolytic or homolytic according as the intermediate ion preferentially splits off a carbonium ion or nitric oxide. The structural circumstances which may determine this choice are briefly considered: the larger nuclear charge of oxygen than of nitrogen will evidently produce a relatively greater predisposition to the loss of a cation, *i.e.*, to the heterolytic process.

(I) *Background and Plan.*

We shall make it probable in this paper that the nitration of derivatives of aniline may pursue paths generally similar to those taken by the nitration of derivatives of phenol (Part VI, *J.*, 1950, 2628), but that certain additional complications arise. Evidence will be adduced in favour

of the conclusion that the nuclear nitration of derivatives of aniline by means of nitric acid takes place by two mechanisms, one of which can proceed in the absence of nitrous acid, whilst the other is dependent on nitrous acid; that these two mechanisms often operate simultaneously; and that side reactions may occur, some of which are oxidative, producing nitrous acid, which influences both nitration mechanisms, especially the second; and that, with tertiary alkylated anilines, dealkylation is a frequent concomitant of nitration. All this is clearly parallel with the phenomena associated with the nitration of derivatives of phenol, as elucidated in Part VI. However, the nitration of derivatives of aniline involves yet further complexities. The chief of these arise, first, from the considerable basicity of aromatic amines, and their tendency to react in cationic forms in strongly acid conditions; secondly, from the ready formation and moderate stability of nitramines and nitrosamines, the production of which may sidetrack, or alternatively constitute a step in, the processes leading to nitration of the aromatic nucleus; and thirdly, from the incursion of an additional dealkylation mechanism.

The great variety of phenomena which come under observation in connection with the nitration of derivatives of aniline has upset our usual plan of studying reaction products and kinetics simultaneously; for much exploratory work on the products of these nitrations had to be done before convenient component processes could be isolated sufficiently completely to render a kinetic investigation profitable. On this account, our kinetic work on the nitration of derivatives of aniline has fallen behind the related work on reaction products; the kinetic work is not yet complete enough to be published. On the other hand, the work on the products is reported at this time, because the observations are sufficiently numerous and diverse to allow some conclusions concerning mechanism to be drawn, even without the support of kinetics, especially since we have the more complete work of Part VI on the nitration of derivatives of phenol to guide our interpretations.

The leading example in which we have studied this problem is the nitration of dimethylaniline. A tertiary base has the advantage that, when no dealkylation occurs, one knows that nitramines and nitrosamines could not have been formed as intermediates. However, a study of the nitration of dimethylaniline requires comparisons of some of the observed phenomena with those involved in the nitration of methylaniline and of aniline, and of the derived nitramines and nitrosamines.

There is a copious previous literature of the nitration of dimethylaniline. Our experiments are mainly complementary to the recorded observations, and must be considered in the setting the latter provide.

(2) *Observations on the Mono- and Di-nitration of Dimethylaniline.*

(2.1) *Nitration in Sulphuric Acid and in Nitric Acid.*—When dimethylaniline is nitrated by nitric acid in an excess of concentrated sulphuric acid, the main first product is *m*-nitrodimethylaniline, and the chief by-product is *p*-nitrodimethylaniline (van Romburgh, *Rec. Trav. chim.*, **1883**, **2**, 108; *Proc. K. Akad. Wetensch. Amsterdam*, **1899**, **2**, 342; Groll, *Ber.*, **1886**, **19**, 198; Noelting and Foumouse, *Ber.*, **1897**, **30**, 2930). According to van Romburgh, it is necessary to dilute the nitration solution with excess of aqueous alkali in order to isolate these mononitration products; for if the solution is diluted with water, further nitration takes place. In this event the *m*-nitrodimethylaniline is converted into 2 : 5- and 3 : 4-dinitrodimethylaniline, whilst the *p*-nitrodimethylaniline is transformed into 2 : 4-dinitrodimethylaniline.

As Groll first recognised, a main product of the nitration of dimethylaniline in a large excess of concentrated nitric acid is *m*-nitrodimethylaniline (Groll, *loc. cit.*; cf. Noelting and Collins, *Ber.*, **1881**, **14**, 261; Noelting, *ibid.*, p. 543).

(2.2) *Nitration by Nitric Acid in Organic Solvents.*—The nitration of dimethylaniline by nitric acid in various concentrations in ether has been studied by Lang (*Compt. rend.*, **1948**, **226**, 1381). He found that part of the material became oxidised to give tetramethylbenzidine and other products, along with nitrous acid. His first simple substitution product was *p*-nitrosodimethylaniline, which was formed after an induction period. With a more concentrated nitration solution, or at a higher temperature, this substance became oxidised to *p*-nitrodimethylaniline. In subsequent steps the last-named compound became converted into 2 : 4-dinitrodimethylaniline, and then into substances involving demethylation—a process to be considered later.

The nitration of dimethylaniline by nitric acid in acetic acid as solvent has been investigated by Weber (*Ber.*, **1877**, **10**, 761), and by Mertz and Weith (*ibid.*, p. 673). The first of these authors obtained *p*-nitrodimethylaniline as the main product. The other investigators used a more concentrated nitration solution, and found the main product to be 2 : 4-dinitrodimethyl-

aniline. We have examined the nitration of dimethylaniline in acetic acid with a view to detecting initial products, and establishing conditions for mononitration.

Dimethylaniline was treated, in 10% solution in acetic acid for 24 hours at room temperature, with varying quantities of 70% nitric acid containing nitrous acid. The proportions of nitric acid ranged from 1·0 to 1·5 mols. per mol. of dimethylaniline. Near the lower end of this range, much dimethylaniline remained unconverted under the conditions used; but by careful chromatography small amounts of *p*-nitrosodimethylaniline and a dinitrotetramethylbenzidine were isolated.

It is usually rather easy to separate the stages of successive nitration of a benzene derivative; but it seems very difficult to effect a clean separation of the mononitration from the dinitration of dimethylaniline. As the proportion of nitric acid was gradually increased in these experiments, unconverted dimethylaniline, and green nitroso-compounds, disappeared in succession from the products; and, simultaneously, mononitrodimethylanilines, and 2 : 4-dinitrodimethylaniline, successively appeared in the products. With 1·4 mols. of nitric acid per mol. of dimethylaniline, no unconverted dimethylaniline remained, and only small amounts of nitroso-compounds were present, whilst the formation of 2 : 4-dinitrodimethylaniline did not assume large proportions. These were judged to be the best conditions for mononitration.

By a combination of distillation and crystallisation, the main constituents of the product obtained under these conditions * were separated, in the following proportions:

o-Nitrodimethylaniline	25 mols. %	Total separated, 75 mols. % of consumed dimethylaniline.
p-Nitrodimethylaniline	39 ,,	
2 : 4-Dinitrodimethylaniline	11 ,,	

o-Nitrodimethylaniline and its *p*-isomeride were now separately treated in 10% solution in acetic acid, under the same conditions as before, with 1·0 mols. of nitric acid per mol. of nitrodimethylaniline. *o*-Nitrodimethylaniline was not affected. *p*-Nitrodimethylaniline was converted almost quantitatively into 2 : 4-dinitrodimethylaniline.

It follows that the 2 : 4-dinitrodimethylaniline, isolated from the product of the attempted mononitration of dimethylaniline, must have been formed entirely by further nitration of *p*-nitrodimethylaniline. The proportions in which the above-described isolation of separated products proves *o*- and *p*-nitro-products to have been originally formed are therefore as follows: *ortho*-, 25%; *para*-, 50% (total isolated, 75%). We have to conclude that, of the successive nitrations, dimethylaniline ⟶ *p*-nitrodimethylaniline ⟶ 2 : 4-dinitrodimethylaniline, the second takes place at a rate comparable to that of the first in our conditions; and also that *p*-nitrodimethylaniline is much more easily nitrated than is its *o*-isomeride. This is discussed in Section 3.

(2.3) *Nitration in Acid–Aqueous Solutions.*—The nitration of dimethylaniline in these conditions has been investigated by Hodgson and his collaborators (Hodgson and Nicholson, *J.*, 1941, 470; Hodgson and Turner, *J.*, 1942, 584; Hodgson, *J. Soc. Dyers and Col.*, 1946, **60**, 151). Aqueous nitrite acidified with hydrochloric acid, in the absence of any added nitric acid, gave *p*-nitrosodimethylaniline, *p*-nitrodimethylaniline, and then the dealkylation product, *N*-nitroso-*p*-nitromethylaniline, to which reference will be made again later. The reaction with 5—10% aqueous nitric acid containing nitrous acid was almost entirely dependent on the presence of the nitrous acid, and it again gave *p*-nitrosodimethylaniline and *p*-nitrodimethylaniline; but in this case there was some oxidation, with the production of 3 : 3′-dinitrotetramethylbenzidine and additional nitrous acid. In 20% aqueous nitric acid the reaction with dimethylaniline proceeded readily without initially added nitrous acid; however, it produced a large amount of 3 : 5 : 3′ : 5′-tetranitrotetramethylbenzidine and nitrous acid; and the rest of the reaction, which led mainly to 2 : 4-dinitrodimethylaniline, obviously depended on this nitrous acid, because it could be inhibited by the addition of urea. The reaction in 40—55% aqueous nitric acid without added nitrous acid, if limited to short periods of time, proceeded without any appreciable oxidation to give nearly quantitative yields of 2 : 4-dinitrodimethylaniline (cf. Mertens, *Ber.*, 1877, **10**, 995); but on prolonged treatment, dealkylation with oxidation set in. With greater concentrations of nitric acid, processes involving dealkylation and oxidation assumed increased importance. These processes not only produced nitrous acid: they were also dependent on nitrous acid, pre-existing or produced, since they were retarded by the presence of urea.

The nitration of dimethylaniline by nitric acid in aqueous sulphuric acid has been studied

* The ratio of the isomeric mononitro-products is likely to be sensitive to the experimental conditions. This matter is being investigated.

by Schuster and Pinnow (*Ber.*, 1896, **29**, 1053) and by Koch (*Ber.*, 1897, **30**, 2851). Their chief product was 2 : 4-dinitrodimethylaniline; but Pinnow showed (*Ber.*, 1899, **32**, 167) that some *o*-nitrodimethylaniline was also formed.

(3) *Discussion of the Mono- and Di-nitration of Dimethylaniline.*

(3.1) ***The Main Routes to Nitration.***—Several nitration routes have to be distinguished. Each is related to the conditions of nitration; and each leads to different consequences.

One nitration route is isolated by the use of a medium of such a high acidity-function that nitration through the free amine is excluded, and nitration through the ammonium ion remains the only possibility. Nitration in a system thus deactivated will require the highly reactive nitronium ion in an appreciable concentration, such as can be built up, *e.g.*, in solvent sulphuric acid. Orientation will be mainly towards the *m*-position. The *m*-nitrated ammonium ion is so strongly deactivated that its further nitration, to give mainly a 3 : 5-dinitro-product, has not been observed. The further nitration which van Romburgh observed on adding water to a sulphuric acid solution which contained the *m*-nitro-ammonium ion (Section 2.1), evidently resulted from a reduction in the acidity-function, which permitted nitration through the free *m*-nitro-amine. Consistently, the second nitro-group entered *o*- and *p*-positions with respect to the dimethylamino-group.

Nitration through the free base leads to *o*- and *p*-nitro-products. It seems probable that two mechanisms are able to effect such nitration, one not dependent on nitrous acid, and the other fundamentally involving nitrous acid, just as with the nitration of phenolic ethers and phenols (Part VI). In this paper, as heretofore, we use the term " nitrous acid " to embrace all materials which, after dilution with water, could be collectively estimated as nitrous acid by ordinary analytical methods. Theoretically, we regard such materials, in so far as they do not consist of the nitrosonium ion itself, as carriers or sources of the nitrosonium ion. It is clear from recorded results that the nitration of dimethylaniline, as free base, is much less dependent on nitrous acid (in our generalised sense) when the availability of the nitronium ion, or of the carrier of the nitronium ion, is high, than when it is low (Section 2.4).

In the latter case, when nitration basically depends on nitrous acid, whether initially present or produced by oxidation, it seems established that the primary *p*-substitution product is *p*-nitrosodimethylaniline, which subsequently becomes oxidised to *p*-nitrodimethylaniline (Sections 2.3 and 2.4). Lang has suggested that the substituting agent in this mechanism is the nitrosonium ion (*loc. cit.*). The intermediate formation of a nuclear nitroso-compound has not yet been established for the *o*-nitration, or for the second stage of nitration, of dimethylaniline.

Either mechanism of nitration of the free base can proceed to a second stage, the product of which is 2 : 4-dinitrodimethylaniline. The dimethylamino-group does not usually suffer decomposition until the aromatic nucleus has been deactivated at least to the extent caused by the introduction of two nitro-substituents. However, nitrous acid is a potent reagent for dealkylation, and, when in high concentration, it can, as Hodgson found, dealkylate and nitrosate the dimethylamino-group in the presence of only one nuclear nitro-substituent (Section 2.4).

(3.2) ***Reactivities in Mono- and Di-nitration.***—It is unusual to find, in successive nitration, a second nitro-group entering a benzene ring approximately as fast as the first; but that is what we do find in the reaction sequence, dimethylaniline ⟶ *p*-nitrodimethylaniline ⟶ 2 : 4-dinitrodimethylaniline (Section 2.3). This may mean merely that, because of the greater basic strength of dimethylaniline than of *p*-nitrodimethylaniline, a smaller proportion of the free base is present, under the conditions of nitration, in the former case than in the latter; the influence of the differing electrochemical equilibria might off-set the deactivating effect of the nitro-group on the reactivity of the aromatic nucleus.

One has to explain why the same relationship is not observed in the reaction sequence, dimethylaniline ⟶ *o*-nitrodimethylaniline ⟶ 2 : 4-dinitrodimethylaniline; and, indeed, why *o*-nitrodimethylaniline is further nitrated so much more slowly than is its *p*-isomeride. This we attribute to the steric inhibition, in *o*-nitrodimethylaniline, of the activating electron-displacements originating in the unshared electrons of the dimethylamino-group. For, as scale models show, an *o*-nitro-group will effectively prevent a dimethylamino-group from assuming by rotation that configuration which is most favourable to the conjugation of its unshared electrons with the mobile electrons of the aromatic ring. The steric inhibition by *ortho*-substituents of such conjugation between a dimethylamino-group and a benzene ring is well attested by dipole moments.

(4) *Observations on the Further Nitration of* 2 : 4-*Dinitrodimethylaniline.*

(4.1) *Possible Routes for the Nitration of* 2 : 4-*Dinitrodimethylaniline.*—The chief end-product of the nitration of dimethylaniline by nitric acid was first isolated by Mertens (*Ber.*, 1877, **10**, 995). It was identified by van Romburgh, who showed that it could be obtained by the nitration of methylaniline, and was *N* : 2 : 4 : 6-tetranitromethylaniline (*Rec. Trav. chim.*, 1883, **2**, 108, 304; 1889, **8**, 215). Its formation from both dimethylaniline and methylaniline by nitration with mixtures of nitric and sulphuric acids was reported by Langerscheidt (*Z. Ges. Schiess-Sprengstoff.*, 1912, 445), and its production from dimethylaniline by such a method was described by van Duin (*Rec. Trav. chim.*, 1917, **36**, 111).

Obviously, *N* : 2 : 4 : 6-tetranitromethylaniline must be formed through 2 : 4-dinitrodimethylaniline if the nitrated substance is dimethylaniline, or through 2 : 4-dinitromethylaniline if the starting point is methylaniline. It could not arise if a nitro-group should enter the 3-position during the initial stages of nitration of dimethylaniline, or of methylaniline. It has been shown that *m*-nitration does constitute a first stage in the nitration of both dimethylaniline and methylaniline in some conditions (cf. Sections 2.1, 2.2; cf. Nolan and Clapham, *Sci. Proc. Roy. Dublin Soc.*, 1923, **17**, 219). It has also been shown that, under conditions which preclude *m*-nitration, the formation of 2 : 4-dinitrodimethylaniline represents a well-marked step in the progressive nitration of dimethylaniline, whilst the production of 2 : 4-dinitromethylaniline is likewise a well-defined stage in the nitration of methylaniline (cf. Sections 2.3, 2.4; cf. Desvergnes, *Chim. et Ind.*, 1930, **24**, 785, 1304). Hodgson and Turner (*loc. cit.*) have observed the conversion of 2 : 4-dinitrodimethylaniline by nitric acid into 2 : 4-dinitromethylaniline. Desvergnes (*loc. cit.*) has studied the transformation of the latter substance, by means of mixtures of nitric and sulphuric acid, into *N* : 2 : 4 : 6-tetranitromethylaniline (cf. also Ryan and Sweeney, *Sci. Proc. Roy. Dublin Soc.*, 1923, **17**, 157).

Since the transformation of 2 : 4-dinitrodimethylaniline into *N* : 2 : 4 : 6-tetranitromethylaniline involves changes both in the amino-part and in the aryl part of the molecule, it must proceed in a series of steps; and we have attempted to discover the route, or routes, taken. The same problem has been attacked by Clarkson, Holden, and Malkin, the manuscript of whose paper (*J.*, 1950, 1556) we were allowed to see through the courtesy of Dr. T. Malkin. Account being taken of some slight difference of conditions, these authors' experimental findings appear to be consistent with ours. It is convenient here to set down a list containing, besides the initial and final substances, (I) and (VIII), a set, (II)—(VII), of the more probable intermediates :

(I.)	2 : 4-$(NO_2)_2C_6H_3$·NMe$_2$	(V.)	2 : 4 : 6-$(NO_2)_3C_6H_2$·NMe$_2$
(II.)	·NMeH	(VI.)	·NMeH
(III.)	·NMe(NO)	(VII.)	·NMe(NO)
(IV.)	·NMe(NO_2)	(VIII.)	·NMe(NO_2)

These suggested intermediates, (II)—(VII), are all known substances. As we have mentioned, Hodgson and Turner observed the conversion of (I) into (II). Ryan and Sweeney record the conversion of (II) by nitric acid into (VI) (*loc. cit.*). Lang observed the conversion of both (I) and (II) by nitric acid into both (III) and (VII), and also the conversion of both (II) and (III) by nitric acid into (IV) (*Compt. rend.*, 1948, **227**, 1284). We shall later report the conversion of (I) into (V) (Section 4.4). Thus it will be clear that all the proposed intermediates, (II)—(VII), can be produced, in either one step or several, from (I).

Next it is necessary to ascertain whether any of these proposed intermediates disqualifies itself by inability to behave as required : any of the compounds (II)—(VII) would have to be excluded from the list of possible intermediates, if it did not yield (VIII) as smoothly as (I) does under comparable conditions. We have therefore examined a fixed set of conditions (cf. Section 7.3) involving the use of nitric acid in aqueous sulphuric acid at room temperature; and we have measured the yields of (VIII). The yields were not quite quantitative, the products being not quite pure. We record below a series of corrected yields of (VIII), two corrections having been applied to the directly weighed yields. The first correction is for the solubility of (VIII) in the aqueous medium from which it was collected. The required solubility values were determined experimentally. The yields thus corrected are called " crude yields." The second correction seeks to allow for the impurities included in the crude yields. The proportions in which impurities are present in the weighed products can, in principle, be determined, as mol.-fractions, from the freezing points and cryoscopic constant. They were first obtained in this form by using clearing points and a roughly evaluated constant; and then, in order to produce comparable corrected yields, they were re-expressed as percentages by weight on the basis of the arbitrary assumption that the average molecular weight of the

impurities is the same as the molecular weight of the main product. The resulting deductions on account of impurities having been made from the crude yields, we call the differences " pure yields ":

Initially taken	(I.)	(II.)	(III.)	(IV.)	(V.)	(VI.)	(VII.)
(VIII.) Crude yield (%)	91	97	97	97	100	100	100
(VIII.) Pure yield (%)	75	95	95	95	96	98	96

It will be seen that all the substances (II)—(VII) give better yields of (VIII) than were obtained from (I). It follows that all qualify, with respect to this test, for consideration as possible intermediates. The yield of (VIII) from (I) can be raised by working at higher temperatures, but the spread of the values is less if a general comparison is made in these conditions, and thus the test is less useful.

(4.2) *Nitration of* 2 : 4-*Dinitrodimethylaniline in Aqueous Nitric Acid.*—A part of the evidence we have to offer concerning the course pursued by the nitration of 2 : 4-dinitrodimethylaniline relates to the identification of products which are formed on nitrating this substance, under uniform conditions as to temperature and time, in aqueous nitric acid of a series of concentrations. The main results are set out below:

(I) treated with	" 40% "	" 50% "	" 70% "	" 98% " HNO_3
Product	(II)	(II) and (VII)	(VII)	(VIII)

Here the compositions of aqueous nitric acid are given by volume: for instance, " 40% " acid is the aqueous acid made by mixing 40 vols. of absolute nitric acid with 60 vols. of water.

The chemically simplest of these transformations is that by which 2 : 4-dinitrodimethylaniline (I) is converted into 2 : 4-dinitromethylaniline (II), with elimination of one of the methyl groups. This methyl group passes into oxidised forms, so that nitrous acid is produced in the course of the reaction. We have estimated that at least two molecules of nitrous acid are produced per molecule of 2 : 4-dinitrodimethylaniline converted. It is necessary to allow for this nitrous acid when one is considering whether 2 : 4-dinitromethylaniline could be an intermediate in the formation of the next of the isolated products, *N*-nitroso-2 : 4 : 6-trinitromethylaniline (VII). We find that, when 2 : 4-dinitromethylaniline is treated with " 70% " nitric acid, to which the indicated amount of nitrous acid has been added, the product is *N*-nitroso-2 : 4 : 6-trinitromethylaniline. Since this last substance is smoothly converted by " 98% " nitric acid into *N* : 2 : 4 : 6-tetranitromethylaniline (VIII), each of the changes of the following sequence is established:

$$(I) \longrightarrow (II) \longrightarrow (VII) \longrightarrow (VIII) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

(4.3) *Nitration of* 2 : 4-*Dinitromethylaniline and its* N-*Nitroso- and* N-*Nitro-derivatives in Aqueous Nitric Acid.*—Each of the steps (I) ⟶ (II) and (VII) ⟶ (VIII) results in a localised modification in the molecule. On the other hand, the conversion written (II) ⟶ (VII) involves substitution both in the side chain and in the nucleus, and therefore this process at least must consist of not less than two steps. Their nature can be inferred from Lang's investigation (*Compt. rend.*, 1948, **227**, 1284) of the action of aqueous nitric acid containing nitrous acid or 2 : 4-dinitromethylaniline (II). He found this substance to be converted by 40% nitric acid into *N*-nitroso-2 : 4-dinitromethylaniline (III). He further found, in agreement with a result given above, that his factor and product (II) and (III) were each converted by nitric acid, in higher concentrations up to 70%, into *N*-nitroso-2 : 4 : 6-trinitromethylaniline (VII). These additional data permit the sequence of reactions (1) to be expanded to the following:

$$(I) \longrightarrow (II) \longrightarrow (III) \longrightarrow (VII) \longrightarrow (VIII) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Each step in this expanded sequence involves only one localised molecular change, and, though this does not mean that every step is necessarily constituted as a single chemical process, it does nevertheless seem probable that one route by which 2 : 4-dinitrodimethyaniline can be transformed into *N* : 2 : 4 : 6-tetranitromethylaniline has been traced in outline.

By the use of nitric acid in concentrations higher than 70%, Lang observed (*loc. cit.*) some conversion of both 2 : 4-dinitromethylaniline (II) and *N*-nitroso-2 : 4-dinitromethylaniline (III) into *N* : 2 : 4-trinitromethylaniline (IV). This suggests the possibility that an alternative reaction path from (I) to (VIII), proceeding *via* (IV), might be utilised in concentrated nitric acid. We have completed the evidence for the feasibility of such a route by showing that (IV) can be converted into (VIII) by nitric acid in concentrations above 70% (and even by hot 50% nitric acid). Thus the separate stages of the following sequence are established:

$$(I) \longrightarrow (II) \longrightarrow (IV) \longrightarrow (VIII) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Each of these stages could represent a single chemical change; but the first and the last of them could alternatively each constitute the over-all result of a double change, as will be discussed in Sections 4.5 and 4.6.

It has been mentioned earlier that our kinetic experiments are too incomplete to be reported yet. However, it is relevant to remark that, at nitric acid concentrations near 90%, the rates of the conversions (II) ⟶ (VIII) and (IV) ⟶ (VIII) have been found to be identical. This confirms the common involvement of (II) and (IV) in the same chain of reactions; and it shows that, at the concentrations mentioned, the reaction route *via* (IV), which is provisionally represented by sequence (3), completely supersedes the route which by-passes (IV), and is represented by sequence (2).

(4.4) *Nitration of* 2 : 4-*Dinitrodimethylaniline by Nitric Acid in Aqueous Sulphuric Acid.*— We have investigated the identity of the products which are formed when 2 : 4-dinitrodimethylaniline is nitrated by nitric acid in aqueous sulphuric acid media of various compositions. Into each aqueous sulphuric acid medium, the nitrating agent was introduced, usually in several proportions, either in the form of nitric acid, or as urea nitrate, the purpose of the latter being to suppress nitrous acid. In presenting the results, we express the compositions of the aqueous sulphuric acid media as percentages by volume, " 50% " medium, for example, being one made by mixing equal volumes of anhydrous sulphuric acid and water. The proportions of nitrating agent, whether added in the form of nitric acid or of urea nitrate, are given as the number of molecules introduced per molecule of 2 : 4-dinitrodimethylaniline. With this explanation, we summarise the main results as follows :

Aq. H_2SO_4 medium	" 50% "		" 55—85% "	" 70% "	" 95% "		
HNO_3 (mols.)	2	5—10	2—10	—	1—3	—	10
Urea-HNO_3 (mols.)	—	—	—	1—5	—	1—3	—
(I) recovered	none	none	some	all	some	some	none
Product	(II)	(VII)	(VIII)	none	(V)	(V)	(VIII)

It is immediately apparent from these data that at least two different routes from 2 : 4-dinitrodimethylaniline (I) to *N* : 2 : 4 : 6-tetranitromethylaniline (VIII) are under observation. In " 50% " sulphuric acid, the isolated intermediates are 2 : 4-dinitromethylaniline (II) and *N*-nitroso-2 : 4 : 6-trinitromethylaniline (VII), just as in not very concentrated aqueous nitric acid (Section 4.2). In outline, this route is as follows :

$$(I) \longrightarrow (II) \longrightarrow (VII) \longrightarrow (VIII) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The nature of the process occurring over the range " 55—85% " of sulphuric acid concentrations does not appear in the results given above; but we add some notes hereunder which point to the conclusion that, like the reaction in the " 50% " medium, the process which predominates over most of the range of media " 55—85% " starts with demethylation of the side chain. It does not follow that the subsequent steps are the same, and we shall show in the next Section that they are not.

In " 95% " sulphuric acid the reaction route is completely different. The first step is now the entry of the third nitro-group into the aromatic nucleus to give 2 : 4 : 6-trinitrodimethylaniline (V). Only after that does modification occur in the side chain. Provisionally this route is represented as follows :

$$(I) \longrightarrow (V) \longrightarrow (VIII) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Three types of observation bear on the general nature of the reaction sequence over the intermediate range " 55—85% " of sulphuric acid compositions. The first has reference to the facility with which (VIII) is produced. Within the range of media " 55—85% " it was noticed that, whilst in a " 55% " medium an initial supply of only two molecular proportions of nitric acid brought about a substantial conversion of (I) into (VIII), the same amount of nitric acid produced very little reaction in a " 60% " medium, or in still more strongly acid media. Furthermore, with reference to the whole series of investigated media, it was observed that, at the extremes of the range, *i.e.*, in the " 50% " medium, and in the " 95% " medium, reaction was effected by lower concentrations of nitric acid, and, for a fixed concentration of nitric acid, reaction was more extensive, than in media of intermediate composition. From this it appears that the reaction routes which start with dealkylation are favoured in aqueous, and not too strongly acid, conditions, whilst the route which commences with nuclear nitration is assisted by strongly acidic conditions. We conclude that, in media of intermediate composition, there is not enough water to facilitate initial demethylation, and too much to be favourable to initial nuclear nitration, so that reaction by both routes is rendered more or less difficult.

The second group of observations relates to the strong purple colour which was observed to be developed during the course of all nitrations, which yielded (VIII), in aqueous sulphuric acid media of lower acid concentration than " 80% ." In this " 80% " medium only a weak purple colour developed. In the " 85% " and " 95% " media no purple colour appeared. Now we have noticed that purple colours in general appear when (II), or (III), or (IV) is being nitrated to give (VIII); but that they do not appear when (V), or (VI), or (VII) is being converted into (VIII); and that they are not given by (VIII) itself; and also that they are not formed when (II), and (III), and (IV) are being interconverted among themselves, without transformation into (VIII). Obviously the production of the colour requires, *inter alia*, the presence of a nuclear position which is still available for substitution, and the existence of conditions in which it can be substituted. (Perhaps the source of the colour is a diaryloxidoammonium ion—cf. Part VI.) For these reasons, we interpret the observations on the conditions of appearance of the colour in the present series of experiments as meaning that the reaction routes which start with demethylation, and which therefore certainly pass through (II), and presumably through either (III) or (IV) or both, are in fact followed in aqueous sulphuric acid media having acid concentrations almost up to " 85% ," although near the upper end of this concentration range, *e.g.*, in an " 80% " medium, these reaction routes are not the only ones which are pursued.

The third set of observations relates to the action of urea. This material completely inhibits reaction in the " 70% " medium, but exerts no such repressive effect on the reaction in the " 95% " medium. From the first of these two observations we draw two conclusions. One is that the initial demethylation depends upon nitrous acid. The other is that the reaction routes which start in this manner are the only routes utilised in aqueous sulphuric acid media having acid concentrations up to at least " 70% ." (These routes continue, as we have seen, to retain some importance in media with acid concentrations up to " 85% ".) From the second of the observations we conclude that the nuclear nitration, which constitutes the initial step of the reaction sequence in the " 95% " medium, does not depend upon nitrous acid.

(4.5) *Nitration of* 2 : 4-*Dinitromethylaniline and of its* N-*Nitroso-* and N-*Nitro-derivatives by Nitric Acid in Aqueous Sulphuric Acid, and the Interconversion of the Three Compounds in Aqueous Acids.*—A simple experiment, which had yielded a substantial amount of information about the chain of reactions which succeeds initial demethylation in the nitration of 2 : 4-dinitrodimethylaniline by nitric acid in a " 70% " aqueous sulphuric acid medium, involves adding *N*-nitroso-2 : 4-dinitromethylaniline (III) to the nitrating acid at room temperature, and watching the colour changes. The original nitrosamine (III) is pale yellow. When it was put into the acid, it instantly turned bright orange, and began to dissolve, forming an orange solution. The colour of this solution faded rather quickly and, after about one minute, the solution suddenly became cloudy with the separation of a pale yellow solid. For a short time the deposition of this continued. Later, the colour of the solution deepened again, passing gradually into an intense purple; and meanwhile the pale yellow precipitate redissolved, and a new, nearly colourless, crystalline substance separated, the complete series of changes requiring about three hours. At each of the stages indicated by a colour change, or by the appearance or disappearance of a precipitate, a part of the solution or mixture was poured into water, and the product was isolated. In this way it was found that the orange substance was 2 : 4-dinitromethylaniline (II), that the pale yellow precipitate was *N* : 2 : 4-trinitromethylaniline (IV), and that the nearly colourless substance was *N* : 2 : 4 : 6-tetranitromethylaniline (VIII). Similar experiments were made starting, not with the nitrosamine (III), but the secondary base (II), and again with the nitramine (IV). The results were the same, except for the expected absence of the earlier reaction stages. Thus (II) was converted successively into (IV) and (VIII); also (IV) was converted into (VIII). The appearances marking these changes were as already described.

The first of the above results shows that the nitrosamine (III) is instantly acidolysed to the secondary base (II), in a medium which is strongly acidic, and not too concentrated with respect to nitrous acid. This has been confirmed in several ways. The nitrosamine (III) has been converted into the secondary base (II) by means of hydrochloric acid either in aqueous solution or in ether, by nitric acid in water or in acetic acid, and by sulphuric acid in water or acetic acid. In the denitrosation with hydrogen chloride in ether, the " nitrous acid " has been trapped and exhibited, by carrying out the reaction in the presence of dimethylaniline and isolating *p*-nitrosodimethylaniline as well as the secondary base (II).

On the other hand, Lang has shown (*Compt. rend.*, 1948, **227**, 1284) that the secondary base (II) is readily transformed into the nitrosamine (III) in an aqueous nitric acid which is not too concentrated with respect to nitric acid, but contains a large concentration of nitrous acid

(Section 4.3). We must conclude that the reaction (II) ⟶ (III) is rapidly reversible in nitrating conditions, the position of equilibrium in a given medium depending on the balance between the activity of the proton carriers (acids), and of the nitrosonium ion carriers (" nitrous acid "), which are present in the medium.

This conclusion affects our view of the reaction sequences (2), (3), and (4), which, in Sections 4.3 and 4.4, were developed to represent routes utilised in the nitration of 2 : 4-dinitrodimethylaniline in somewhat dilute nitric acid, in more concentrated nitric acid, and in moderately dilute aqueous sulphuric acid, respectively. In each of these sequences, the first stage, written (I) ⟶ (II), expresses an initial formation of the secondary base (II) by the demethylation process. But, as Hodgson showed (cf. Section 2.4) for demethylation in aqueous nitric acid, and as we have shown (Section 4.4) for demethylation in aqueous solutions containing both nitric and sulphuric acids, these aqueous demethylations are basically dependent on nitrous acid. It is therefore chemically reasonable to suppose that the primary product might be the nitrosoamine (III). This being so, our observations, establishing the mobile equilibrium (II) ⇌ (III), open the possibility that what was taken to be the stage (I) ⟶ (II) in the reaction schemes (2), (3), and (4), might represent an overall result of the two stages (I) ⟶ (III) ⇌ (II). This possibility remains open independently of whether further reaction takes place through (II), as in the sequences (3) and (4), or through (III), as in the sequence (2). We shall return to this question in Sections 5.1, 6.1, and 6.2.

Another result of the described experiment is that the secondary base (II) is readily nitrated by nitric acid in " 70% " aqueous sulphuric acid to give the nitramine (IV). Lang made a corresponding observation for nitration by moderately concentrated nitric acid (*cf.* Section 4.3). Lang demonstrated the reverse reaction, by showing that the nitramine (IV) became denitrated in aqueous sulphuric acid, to give back the secondary base (II) (*Compt. rend.*, 1948, **227**, 1284). We have made similar observations using other aqueous strong acids, such as hydrochloric acid, as is reported in Part VIII (following paper). It must therefore be concluded that the secondary base and the nitroamine are reversibly interconvertible in acidic nitrating conditions, the position of the equilibrium (II) ⇌ (IV) depending on the relative activities with which proton carriers (acids) and nitronium ion carriers (" nitric acid ") are present in the medium employed. By suppressing one or other of these types of reagent, we can make the conversion substantially irreversible in either direction. Now by treating (IV) with an aqueous strong acid, in the initial absence of nitric acid, and therefore at a low average concentration of nitric acid, we have rendered the denitration (IV) ⟶ (II) nearly quantitative (*ibid.*). Again, by subjecting (II) to nitrating conditions in the initial absence of acid, for instance, by treating (II) with dinitrogen pentoxide in chloroform, or with " acetyl nitrate " in acetic anhydride (cf. Parts IV and V, *J.*, 1950, 2452, 2467), we have made the *N*-nitration nearly quantitative (*ibid.*). Thus reversibility in the nitration–denitration system (II) ⇌ (IV) is established, just as is that of the nitrosation–denitrosation system (II) ⇌ (III). However, there is a very distinct kinetic difference between the two systems; for under the conditions in which we have attempted to follow the course of the nitration of 2 : 4-dinitrodimethylaniline, the reversible nitration (II) ⇌ (IV) reaches equilibrium much less rapidly than does the reversible nitrosation (II) ⇌ (III).

The circumstance that the system (II) ⇌ (IV) involves (II), which is also a member of the more mobile system (II) ⇌ (III), presents us with the problem of determining whether it is really (II), rather than (III), which is converted into, and is formed from, (IV). For example, nothing in the observations so far mentioned distinguishes between the direct forward change (II) ⟶ (IV), and a sequence of two changes (II) ⇌ (III) ⟶ (IV), fulfilling the condition that the first is rapid and strongly reversed, while the second is slow. The following is an attempt to solve this problem.

The suggested unit process (III) ⟶ (IV) can conceivably occur in only two ways, *viz.*, (1) as a direct oxidation, $>N{\cdot}NO \longrightarrow >N{\cdot}NO_2$, and (2) as a single-stage bimolecular substitution $NO_2^+ + >N{\cdot}NO \longrightarrow >N{\cdot}NO_2 + NO^+$. We shall adduce reasons for believing that, in fact, it does not take place by either of these mechanisms. We think that it cannot proceed by oxidation, because we have attempted to effect the conversion with other strong oxidising agents, such as hydrogen peroxide and Caro's acid, but with complete lack of success. We think that it cannot proceed by substitution, because, under our usual nitration conditions, the equilibrium (II) ⇌ (III) is strongly on the side of (II); and therefore an *N*-nitrating substitution in this system would proceed through (III) rather than through (II), only if it were intrinsically much easier in electrophilic substitution to effect the expulsion of a nitrosonium ion, than of a proton, from combination with the nitrogen atom of the amine. This seems an

impossible assumption, whether one bases one's views on experience of proton transfers in general, or on the more specific ground that, even in aromatic *C*-nitration, protons are ejected rapidly (Part II, *J.*, 1950, 2400). Therefore we conclude that the interconversion of (III) and (IV) does not take place directly, but proceeds by way of (II):

$$\text{(III)} \rightleftharpoons \text{(II)} \rightleftharpoons \text{(IV)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

In the course of these experiments with the nitrosamine (III), we have observed no sign of its isomerisation in the presence of acids to 2-nitroso-4:6-dinitromethylaniline. The effect of acids on (III) is to denitrosate it to (II), not to isomerise it. The conclusion is that isomerisation of the nitrosamine does not contribute to the series of changes with which we are now concerned. The nitramine (IV) is in a different case: for, as we shall indicate in Section 4.6, it is isomerised by acids in certain conditions to 2:4:6-trinitromethylaniline (VI).

A result of the various observations reported in this Section is that we are now in a position to set down an outline scheme for the nitration of 2:4-dinitrodimethylaniline in "70%" aqueous sulphuric acid. It is as follows:

$$\text{(I)} \longrightarrow \text{(III} \rightleftharpoons \text{II)} \longrightarrow \text{(IV)} \longrightarrow \text{(VIII)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

Route (7) for nitration in "70%" sulphuric acid is essentially identical with route (3) for the reaction in concentrated nitric acid. In route (7), as in route (3), the change (IV) ⟶ (VIII), which we have yet to discuss in detail, is not necessarily a single process.

(4.6) *The Rearrangement of N:2:4-Trinitromethylaniline in Sulphuric Acid Media and its Nitration by Nitric Acid.*—One of the two types of nitration media, in which a route for the nitration of 2:4-dinitrodimethylaniline has been diagnosed which proceeds through the nitroamine (IV), is aqueous sulphuric acid in concentrations near "70%" (Section 4.6).

Lang has reported (*Compt. rend.*, 1948, **227**, 1284) that *N*:2:4-trinitromethylaniline (IV) is converted by 96% sulphuric acid into its rearrangement product, 2:4:6-trinitromethylaniline (VI). We find (cf. Part VIII) that in concentrated sulphuric acid this transformation is instantaneous, but that in "70%" aqueous sulphuric acid it is measurably slow, requiring, for instance, several hours at the ordinary temperature to proceed substantially to completion.

The transformation of (IV) into (VI) is intramolecular: it does *not* consist of a denitration followed by a re-nitration, (IV) ⟶ (II) ⟶ (VI). These conclusions are fully established in Part VIII (following paper).

If nitric acid is added to the solution which is obtained by allowing (IV) to be converted into (VI) in "70%" aqueous sulphuric acid, or if it is added to a solution prepared by dissolving the isolated compound (VI) in the "70%" acid, then the compound (VI) is rapidly nitrated to give *N*:2:4:6-tetranitromethylaniline (VIII). This reaction is sufficiently facile to secure that, if (VI) were formed by rearrangement of (IV) in "70%" aqueous sulphuric acid, in the presence of an adequate supply of nitric acid added initially, then the product isolated would be (VIII).

The rate of the overall conversion of (IV) into (VIII) in "70%" aqueous sulphuric acid containing nitric acid is of the same order of magnitude as the rate of the conversion of (IV) into (VI) in the "70%" sulphuric acid without the nitric acid. It is therefore of the same order of magnitude as the rate of the conversion of (IV) successively into (VI) and (VIII) in the "70%" sulphuric acid containing nitric acid, since the second of the two reactions is much faster than the first. The evidence is therefore complete that, under the conditions in which the change (IV) ⟶ (VIII) has been observed in "70%" aqueous sulphuric acid, much of the reaction must, and all of it may, pursue the two-stage sequence

$$\text{(IV)} \longrightarrow \text{(VI)} \longrightarrow \text{(VIII)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

The step (IV) ⟶ (VI) is irreversible. The step (VI) ⟶ (VIII) is reversible, but we shall be discussing this in Section 4.7.

The other type of medium, in which a route for the nitration of 2:4-dinitrodimethylaniline has been detected which proceeds through *N*:2:4-trinitromethylaniline (IV), is aqueous nitric acid of concentration not less than "70%" (Section 4.3). In this case our evidence concerning the nature of the reaction by which *N*:2:4-trinitromethylaniline is converted into *N*:2:4:6-tetranitromethylaniline (VIII) is not complete. The difficulty is that we cannot study the rearrangement of *N*:2:4-trinitromethylaniline to 2:4:6-trinitromethylaniline (VI) in isolation, because of the great rapidity with which the last-named substance is nitrated to *N*:2:4:6-tetranitromethylaniline in the nitric acid medium. All we can show is that the nitration (VI) ⟶ (VIII) is sufficiently fast compared with the overall conversion

(IV) ⟶ (VIII) to allow it to be supposed that the reaction follows the two-stage sequence (8). Kinetic measurements which establish these comparisons will be reported later.

(4.7) *Interconversion of* 2 : 4 : 6-*Trinitrodimethylaniline,* 2 : 4 : 6-*Trinitromethylaniline,* N-*Nitroso*-2 : 4 : 6-*trinitromethylaniline, and* N : 2 : 4 : 6-*Tetranitromethylaniline.*—In " 95% " aqueous sulphuric acid, the nitration of 2 : 4-dinitrodimethylaniline pursues a different course from any that has been established for nitration in more aqueous solutions : in the concentrated acid the initial process is not demethylation, but nuclear nitration to form 2 : 4 : 6-trinitrodimethylaniline (V) (Section 4.4). Demethylation and modification of the side chain set in subsequently, and we have now to consider what can be learned about these processes by experimenting with 2 : 4 : 6-trinitrodimethylaniline, and with the products that can be derived from it.

2 : 4 : 6-Trinitrodimethylaniline (V), when treated with 10 mols. of nitric acid in " 95% " aqueous sulphuric acid, was transformed into *N* : 2 : 4 : 6-tetranitromethylaniline (VIII). A similar experiment with " 70% " aqueous sulphuric acid as the medium led to the same result. However, when in this medium the proportion of nitric was reduced to 2 mols., the simple demethylation product, 2 : 4 : 6-trinitromethylaniline (VI), was obtained.

2 : 4 : 6-Trinitromethylaniline (VI) is known to be very easily nitrated to *N* : 2 : 4 : 6-tetranitromethylaniline (VIII). Lang has studied the conversion, using aqueous nitric acid of concentration " 70% " or higher (*Compt. rend.*, 1948, **227**, 1284). We have studied the kinetics of the nitration under such conditions, though this will be reported later. We have also employed, as nitrating agent, solutions of nitric acid in aqueous sulphuric acid media of concentration " 55% " or higher. Under these conditions the reaction is appreciably reversible, as is shown by the following experiments.

Lang has reported the denitration of *N* : 2 : 4 : 6-tetranitromethylaniline to 2 : 4 : 6-trinitromethylaniline by the action of sulphuric acid (*loc. cit.*). We have observed the same reaction in aqueous sulphuric acid; and, using aqueous sulphuric acid containing nitric acid, we have followed the attainment of equilibrium from either side in the balanced reaction (VI) ⇌ (VIII). The equilibrium depends on the acidity of the medium in relation to its nitrating power, *i.e.*, on the conflict between carriers of the proton and those of the nitronium ion. A rise of temperature appears to favour denitration.

These observations establish the following reaction sequence, which is possibly an adequate representation of the processes by which the side chain of (V) may be modified in the experimental conditions in which (V) is known to be formed during the nitration of 2 : 4-dinitrodimethylaniline in aqueous sulphuric acid :

$$\text{(V)} \longrightarrow \text{(VI)} \rightleftharpoons \text{(VIII)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

But since the demethylation produces nitrous acid, *N*-nitroso-2 : 4 : 6-trinitromethylaniline (VII) is a possible intermediate product; and therefore its formation from, and conversion into, the compounds involved in scheme (9) require examination.

The nitrosamine (VII) is on the whole more easily produced in nitric acid than in sulphuric acid media. When (V) is demethylated, to produce nitrous acid, by " 70% " aqueous nitric acid, or by " 70% " nitric acid containing initially added nitrous acid, (VII) is formed. We have observed that, when (VII) is treated with " 70% " nitric acid for some hours at the ordinary temperature, (VIII) is produced.

The relative rates of these reactions are of interest. We found that, in " 70% " nitric acid containing 0·25—0·75M-nitrous acid, (VI) was converted into (VII) almost completely, and much more rapidly than (VI) was converted into (VIII) in the same aqueous nitric acid without the nitrous acid; and, furthermore, that, with this acid as the initial nitrating medium, (VI) was converted into (VIII) much more rapidly than (VII) was transformed into nitrous acid and (VIII).

Because of the comparative rapidity of the reaction (VI) ⟶ (VII), we cannot tell from these observations whether or not the conversion (V) ⟶ (VII) proceeds by way of (VI) in nitric acid. Again, owing to the comparative rapidity of the reaction (VI) ⟶ (VIII), one cannot deduce from the presented results whether or not the observed change (VII) ⟶ (VIII) takes place by way of (VI) in nitric acid. These questions will, however, be further pursued in Sections 5.1, 6.1, and 6.2.

It has been mentioned that, in nitric acid media, (VI) may be nitrosated to (VII) fairly completely. The denitrosation of (VII) to yield (VI) is easily effected in sulphuric acid media, as has been reported by Lang (*loc. cit.*). It follows that, in strong acids containing nitrous acid,

an equilibrium (VI) ⇌ (VII) will be set up, the position of which must depend on the balance obtaining between the nitrosating power and acidity of the medium, *i.e.*, on the relative availability of nitrosonium ions and protons.

If a solution in which such an equilibrium can be set up is also a nitrating medium, then it should be possible successively to denitrosate (VII) to (VI) and to nitrate (VI) to (VIII) in a single experimental operation. Using " 70% " aqueous sulphuric acid containing nitric acid, we have observed the overall conversion of (VII) into (VIII). But we have been unable either to establish the dissection of the process into stages, or to prove convincingly that it proceeds by an independent one-stage route. The following evidence is submitted for what it is worth. The free amine (VI) has a deep orange-yellow colour, whilst the nitrosamine (VII) is pale yellow, and the nitramine (VIII) is almost colourless. A conversion of (VII) into (VIII) by way of (VI) might have been diagnosed as a two-stage process by an observation of a temporary deepening of the yellow colour during the change, just as was done for the corresponding compounds containing only two nuclear nitro-groups (Section 4.5). In the present case no sign of such a transient deepening of colour could be seen: the pale yellow colour of the nitrosamine faded continuously as the nitramine was produced.

On the basis of these results, we now elaborate scheme (9) as follows:

(10)

However, certain questions which this diagram might be thought to decide are actually held in reserve. For first, it is uncertain whether the changes (V) ⟶ (VII) and (VII) ⟶ (VIII) are independent single-stage processes, or are covered by combinations of the other represented changes. Secondly, if it should be decided that the change (V) ⟶ (VII) is a unit process, then, in the absence of new evidence, we should have to agree that the process (V) ⟶ (VI) might, or might not, be single; for the balanced system (VI) ⇌ (VII) is probably mobile enough to permit the appearance of either of the participating compounds under the conditions of their observed production, even if only one route should exist from (V) into the mobile system.

(5) *Observations on the Demethylation of* 2 : 4-*Dinitrodimethylaniline and* 2 : 4 : 6-*Trinitrodimethylaniline during Nitration.*

(5.1) *Dealkylation of Alkylated Derivatives of Aniline by Nitric Acid, by Nitrous Acid, and by Dinitrogen Tetroxide.*—We refer first to the investigation, described in Part VI (*J.*, 1950, 2628), concerning the dealkylations which accompany the nitration of phenolic ethers. It was shown that the methyl group of *p*-chloroanisole is in part eliminated during the nitration of this substance in conditions in which the substitution does not depend on nitrous acid; and that the group is eliminated more extensively during nitration in other conditions in which the total reaction fundamentally depends on nitrous acid. The methyl group was recovered as methyl acetate after nitration in acetic acid as solvent; this shows that it was eliminated in a non-oxidised form. On the other hand, the ethyl group eliminated during the nitration of *p*-chlorophenetole in similar conditions became oxidised.

Other workers have established the general tendency to the elimination of one, but only one, alkyl group during the nitration and nitrosation of dialkylanilines, and also the tendency of the group to be eliminated in an oxidised form. Reilly and Hickinbottom (*J.*, 1920, **117**, 135) studied the nitration of methyl-*n*-butyl-, ethyl-*n*-butyl-, and di-*n*-butyl-aniline by an excess of fuming nitric acid and acetic acid. In each case the aromatic product was an *N* : 2 : 4 : 6-tetranitroalkylaniline, one alkyl group having been eliminated. In the example of di-*n*-butylaniline, the same product was obtained when the nitrating agent was a mixture of nitric acid and sulphuric acid, and in this case butyric acid also was recovered. Davidson and Reade (*J.*, 1939, 1701) examined the action of nitrous acid on dimethylaniline-*p*-sulphonic acid. They obtained *N*-nitroso-*p*-nitromethylaniline. Nitric oxide was evolved, and the eliminated methyl group was recognised as formaldehyde. Hodgson and Nicholson (*J.*, 1941, 470) studied the actions of nitrous acid on other dialkylanilines, establishing Et > Me > CH_2Ph as the order of ease of elimination of the alkyl group.

We have noticed in a number of examples that the dealkylation of a dialkylaniline in nitric acid media is strongly accelerated by added nitrous acid. This has been demonstrated for the

transformation of 2 : 4-dinitrodimethylaniline (I) into *N* : 2 : 4-trinitromethylaniline (IV) by anhydrous nitric acid in acetic acid. It has been established for the conversion of 2 : 4 : 6-trinitrodimethylaniline (V) into *N* : 2 : 4 : 6-tetranitromethylaniline (VIII) by nitric acid in " 90—95% " aqueous sulphuric acid. It is concluded that nitrous acid is a much more powerful dealkylating agent for aromatic tertiary amines than is nitric acid. Furthermore, it appears that, since all these alkyl eliminations involve oxidation with the production of nitrous acid, this material is likely to be by far the most effective, perhaps the only effective, dealkylating agent present in our nitrating conditions.

Whereas sodium nitrite (5 mols.), when added to a solution of 2 : 4-dinitrodimethylaniline (I) in concentrated sulphuric acid at room temperature, had little demethylating action, the subsequent addition of water to produce a " 70% " acid, or a somewhat more dilute acid, resulted in a rapid reaction, which produced *N*-nitroso-2 : 4-dinitromethylaniline (III) with loss of a methyl group. Similar effects were observed on starting with 2 : 4-dinitrodiethylaniline, which, after the same treatment, produced *N*-nitroso-2 : 4-dinitroethylaniline. We take these results to mean that the process of dealkylation by nitrous acid requires the free amine, and that it is inhibited in a medium having so high an acidity function that conversion of the base into the ammonium salt is complete.

Dinitrogen tetroxide in organic solvents effected the dealkylation of 2 : 4-dinitrodimethylaniline and 2 : 4-dinitrodiethylaniline in a particularly smooth manner; and there was an interesting difference in the nature of the product according to the solvent used. When acetic acid was the solvent, the products were what they would have been if dealkylation had been effected by nitrous acid in an aqueous acid medium: they were the *N*-nitroso-2 : 4-dinitroalkylanilines. However, when chloroform was the solvent, the products were the 2 : 4-dinitroalkylanilines. Since these secondary amines were rapidly nitrosated by dinitrogen tetroxide in acetic acid to give the *N*-nitroso-compounds, whereas the latter could not be denitrosated by dinitrogen tetroxide in chloroform to give the amines, we have, for a restricted range of conditions, an answer to the question of whether the secondary amine or the nitrosoamine is the more immediate dealkylation product: clearly, the secondary amine is, for it is formed in conditions in which the nitrosoamine is the thermodynamically stable product. We shall later generalise this conclusion.

We have made some additions to recorded observations concerning the fate of alkyl groups eliminated from tertiary amines in nitrating or nitrosating conditions. It was noted above that an eliminated methyl group has previously been recognised as formaldehyde. We have decomposed 2 : 4-dinitrodimethyl-, 2 : 4-dinitrodiethyl-, and 2 : 4-dinitrodi-*n*-butyl-aniline with aqueous nitric acid containing nitrous acid, and have obtained formaldehyde, acetaldehyde, and *n*-butaldehyde, respectively, each isolated as its 2 : 4-dinitrophenylhydrazone. The least oxidised form in which an eliminated *n*-butyl group has previously been recovered is *n*-butyric acid. It seems natural to regard *n*-butaldehyde as an earlier product. We proved that it was inadmissible to regard *n*-butyl alcohol as a still earlier product by showing that this substance, when placed under comparable conditions, was converted into *n*-butyl nitrite.

In the products of the reactions of dinitrogen tetroxide with 2 : 4-dinitrodimethylaniline and 2 : 4-dinitrodiethylaniline in organic solvents we recognised formaldehyde and acetaldehyde, respectively. On all the evidence, we conclude that aldehydes are the first isolable forms to be assumed by primary alkyl groups eliminated from simple tertiary amines by the action of any of the group of substances which we cover by the term " nitrous acid."

(5.2) *Dealkylation of Alkylated Derivatives of Aniline by Chromic Acid and Permanganic Acid.* —Since the dealkylation of aromatic tertiary amines, as induced by nitrous acid, is closely connected with oxidation, it seemed desirable to compare the dealkylating action of nitrous acid with the oxidising action on tertiary amines of some common oxidising agents such as chromic and permanganic acids.

Some significant facts about the action of chromic acid are already known. Van Romburgh (*Rec. Trav. chim.*, 1889, **8**, 249) examined the behaviour of this reagent towards 2 : 4-dinitrodimethylaniline and 2 : 4-dinitrodiethylaniline. He obtained 2 : 4-dinitromethylaniline and 2 : 4-dinitroethylaniline in the respective cases; and in the second case demonstrated the formation of acetaldehyde. In marked contrast to the reactions with nitrous acid, continued treatment with chromic acid removed the remaining alkyl group from each secondary amine. In agreement with these results, we have found that, whilst 2 : 4-dinitrodiethylaniline, on treatment with a solution of chromium trioxide in acetic acid, lost only one alkyl group giving 2 : 4-dinitroethylaniline and acetaldehyde, the same tertiary amine, on interaction with chromic acid in " 30% " aqueous sulphuric acid, lost both groups yielding 2 : 4-dinitroaniline,

together with acetaldehyde. Pinnow and Wiskott have recorded (*Ber.*, 1899, **32**, 913) that 2 : 4-dinitrodibenzylaniline is degraded to 2 : 4-dinitroaniline, even by a solution of chromium trioxide in acetic acid.

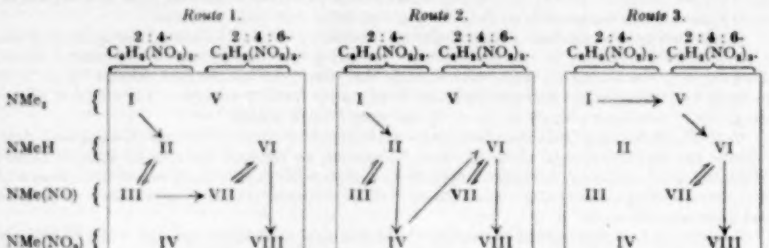
The indication we see here, that benzyl groups are more easily eliminated than ethyl groups in these reactions, is extended in some results obtained by Mulder (*Rec. Trav. chim.*, 1899, **8**, 117), who examined the action of chromium trioxide in acetic acid solution on a number of 2 : 4-dinitrodialkylanilines containing unlike groups and established, *inter alia*, that the benzyl group is eliminated in preference to the methyl group. We should certainly expect the benzyl group to be more vulnerable than either the methyl or the ethyl group, if the seat of the oxidising attack is in the alkyl group itself. But the result forms a second major contrast to what has been found for the oxidative elimination of alkyl groups from tertiary amines by means of nitrous acid, *viz.*, that the benzyl group is less easily eliminated than either the methyl or the ethyl group (Section 5.1). Obviously there is some fundamental difference between the mode of action of chromic acid and that of nitrous acid: we shall later suggest that this difference is connected essentially with the location of the oxidising attack.

The action of permanganic acid on tertiary aromatic amines has been briefly examined. As far as the matter has been pursued, the results suggest analogies with the action of chromic acid, rather than with that of nitrous acid. When a solution of 2 : 4-dinitrodimethylaniline in "35%" sulphuric acid was treated with potassium permanganate, a vigorous reaction set in which produced 2 : 4-dinitromethylaniline and some formaldehyde. A similar experiment with 2 : 4-dinitrodiethylaniline gave 2 : 4-dinitroaniline and acetaldehyde. Thus permanganic acid, like chromic acid, is able to remove both alkyl groups from a dialkylated aromatic amine.

(6) *Discussion of the Further Nitration of* 2 : 4-*Dinitrodimethylaniline.*

(6.1) *Routes followed in the Conversion of* 2 : 4-*Dinitrodimethylaniline into* N : 2 : 4 : 6-*Tetranitromethylaniline.*—In writing this paper we have taken the view that the observations bearing on the course of the further nitration of 2 : 4-dinitrodimethylaniline were too numerous to make it convenient to report them in their entirety before attempting any collation; and therefore in Sections 4 and 5 we have separated the observations into a number of groups, associating with the record of each group a partial interpretation, essentially for the purpose of summarising the data. It now remains to assemble these partial interpretations into a picture of the overall process.

The course of the transformation of 2 : 4-dinitrodimethylaniline into *N* : 2 : 4 : 6-tetranitromethylaniline has been discussed before, but not always with a due appreciation of the circumstances that different routes are followed in different experimental conditions. We think that the evidence which has been accumulated points to three main routes, each probably capable of minor variations. We call the Routes 1, 2, and 3, and they are represented in the diagrams below, the associated legends indicating in an approximate way the types of experimental conditions to which the routes respectively apply.



We must mention the points in which these diagrams make constituent reactions appear more definite than, strictly, the evidence warrants. The first relates to the question of which is the end of the mobile system (II) $\rightleftharpoons$ (III) through which material enters it from (I) in Routes 1 and 2, and, correspondingly, which is the end of the system (VI) $\rightleftharpoons$ (VII) through which

material enters from (V) in Route 3. The diagrams express the opinion that in every case the tertiary amine, on demethylation by nitrous acid, gives first the secondary amine. However, this has been experimentally established (Section 5.1) only for dealkylation in feebly polar solvents, in which the process (I) ⟶ (II) ⟶ (III), for example, can be separated into its stages. Theory enters when we extend this conclusion to demethylation in polar solvents, though the arguments seem good, as we shall hope to show in Section 6.2.

The other main matter which is a little more open than the diagrams suggest is the question of which is the end of the mobile system (VI) ⇌ (VII) through which material leaves it on passing into (VIII). The diagrams represent it to be (VI). The relevant facts are that (VI) is converted much more easily than (VII) into (VIII), even if, as is doubtful, (VII) can be converted at all into (VIII) directly, rather than through (VI). It follows that material will certainly leave the system (VI) ⇌ (VII) by way of (VI) in all circumstances except possibly when the medium is so highly charged with nitrous acid that the system (VI) ⇌ (VII) exists as (VII) to the almost complete exclusion of (VI). In this case it remains doubtful whether (VII) will actually pass into (VIII) by way of (VI) or directly.

Of the three routes described • for the dealkylation and further nitration of 2 : 4-dinitrodimethylaniline, Routes 1 and 2 commence with demethylation, and for this the essential reagent is nitrous acid. The nature of the substituting agent responsible for the subsequent nitration stages is undetermined for Route 1; but it is indirectly indicated to be the nitronium ion for the *N*-nitrations of Route 2. The initial step in Route 3 is *C*-nitration; and here it may be considered certain that the reagent is the nitronium ion.

Recalling the discussion in Section 3, we notice that in the nitration, without demethylation, of dimethylaniline to yield successively *o*- or *p*-nitro-, 2 : 4-dinitro-, and 2 : 4 : 6-trinitro-dimethylaniline, the first and the second nitro-group enter, at least partly, by what, in Part VI, was called the " special " nitration mechanism, and interpreted as arising from aromatic attack by the nitrosonium ion; whilst the third nitro-group cannot be introduced by this substituting agent, but requires the intervention of the " general " nitration mechanism, with its more powerful electrophilic reagent, the nitronium ion.

(6.2) *Mechanism of the Dealkylation accompanying Nitrosation and Nitration.*—We shall here discuss the mechanism of dealkylation by " nitrous acid," using this term in our generalised sense. Much of what has to be said may well apply, with an obvious modification, to the less facile process of dealkylation by nitric acid, when it occurs. We have to keep in mind that dealkylations are prevalent during the nitrosation and nitration of phenolic ethers, as well as in the corresponding reactions of tertiary alkylated aromatic amines.

Our first conclusion is that, within this field as a whole, there are *two* mechanisms of dealkylation. One is especially important for the dealkylation of phenolic ethers. It is non-oxidative. It was observed (Part VI, *J.*, 1950, 2628), free from any accompanying oxidation process, in connexion with the nitrous acid-catalysed nitration of *p*-chloroanisole. It was recognised as heterolytic, and fundamentally allied in mechanism to the well-established heterolyses of 'onium ions. An explanation which was given assumed that the nitrosonium ion adds itself to the oxygen atom of the phenolic ether, thereby causing the loss of a carbonium ion, although later the nitrosonium ion itself is sent away in consequence of the uptake of a proton :

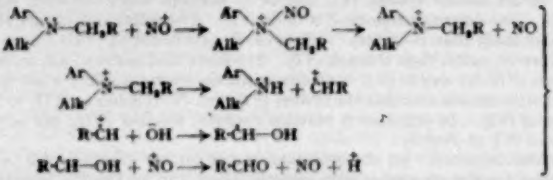
$$\left.\begin{array}{l} \mathrm{Ar{\cdot}OR + NO^+ \longrightarrow Ar{\cdot}\overset{+}{O}\!<\!\begin{matrix}\mathrm{R}\\ \mathrm{NO}\end{matrix} \longrightarrow Ar{\cdot}ONO + R^+} \\ \mathrm{Ar{\cdot}ONO + H^+ \longrightarrow Ar{\cdot}\overset{+}{O}\!<\!\begin{matrix}\mathrm{H}\\ \mathrm{NO}\end{matrix} \longrightarrow Ar{\cdot}OH + NO^+} \\ \mathrm{R^+ + A^- \longrightarrow RA} \end{array}\right\} \quad \ldots\ldots \quad (11)$$

Here A^- is any available anion, taken from a molecule if necessary, for instance, an acetate ion taken from solvent acetic acid. A significant characteristic of this mechanism is the recovery of R as RA.

The other mechanism is oxidative. It is of particular importance for the dealkylation of tertiary amines. We diagnose it as homolytic, and consider that it enters our field of observation, competing successfully with the heterolytic mechanism, essentially for the reason that solvated NO^+ and neutral NO are comparably stable structures differing by one electron, with the consequence that the NO-group can add to any basic centre as NO^+ and come away as NO, thereby carrying off one electron and effecting an oxidation. We assume the first step to be the

• We have to keep in mind that routes may be utilised other than those described. One of the likelier additional routes is one involving the direct nuclear nitration of (IV) to (VIII). We could not discern this, but none of our observations excludes it, or even renders it particularly improbable.

same as is shown for the heterolytic mechanism, *viz.*, the formation of nitrosammonium ion; but now this, instead of losing a carbonium ion, loses neutral nitric oxide (which, in fact, is evolved, unless nitric acid is present in sufficient concentration to oxidise it). The resulting incomplete electron shell is then made good by the internal transfer of a hydrogen atom, and the alkyl group thus disrupted is split off as a radical-cation, which combines with any available anion (*e.g.*, OH^-), and, after losing its odd electron to the oxidising environment (*e.g.*, to NO^+), finishes its career as an aldehyde:



. . . (12)

The chief points (Section 5.1) which a theory of the oxidative mode of dealkylation must explain are (1) why the reaction seems to require the amine itself rather than its cation, (2) why the reaction works with a tertiary amine but not with a secondary one, (3) why the eliminated alkyl group appears as an aldehyde, (4) why the alkyl group most easily eliminated is not necessarily that most prone to oxidation, (5) why the primary dealkylation product, at least in an aprotic solvent, is the secondary amine, even when the thermodynamically stable product is the nitrosoamine, and (6) why this collection of characteristics arises particularly with nitrous acid as the reagent. Answers to all these questions are suggested by the mechanism. (1) The oxidising agent happens to be a typical co-ordinating electrophile with an affinity for basic electron-pairs. (2) The nitrosammonium ion which it forms would immediately lose a proton if the original amine were secondary, and then the remaining reactions would not occur. (3) The mechanism shows why the eliminated alkyl group must appear as an aldehyde. (4) As the oxidising agent does not attack the alkyl group, we should not expect the latter to behave exactly as if it did. (5) The mechanism shows why the primary dealkylation product is the secondary amine, even when the thermodynamically stable product is the nitrosoamine. (6) We have already pointed to the property of " nitrous acid " which we conclude to be responsible for the mechanism and its attendant effects, *viz.*, the stability of *both* NO^+ and NO.

This kind of property is not quite peculiar to nitrous acid. In Part VI evidence was given of the existence of a non-oxidative process of dealkylation of *p*-chloroanisole, which depended on nitric acid, rather than nitrous acid. There is strong reason to think that this reaction pursues a heterolytic course, quite analogous to that outlined in equation (11), excepting that the nitronium ion takes the part there assigned to the nitrosonium ion. Now the solvated nitronium ion and the nitrogen dioxide molecule are more or less comparably stable structures, differing by one electron, and therefore they might participate in an oxidative and homolytic process of dealkylation, similar to that represented in equations (12), except that the nitronium ion and nitrogen dioxide would take the parts assigned in those equations to the nitrosonium ion and nitric oxide, respectively. The difficulty in arranging to observe this reaction is that, once such a process starts, nitrous acid is produced, and then the reactions dependent on nitrous acid obscure the original process. Thus we have, easily susceptible to observation, heterolytic and homolytic mechanisms of dealkylation by nitrous acid, but only the heterolytic mechanism of dealkylation by nitric acid: and all these three observable mechanisms have, in our opinion, been observed.

We have to consider why the heterolytic mechanisms seem especially important for the dealkylation of phenolic ethers, whilst the homolytic process appears to be the principal mechanism utilised for the dealkylation of aromatic tertiary amines. First, it should be noted that the difference is probably one of degree, rather than of kind. Certainly, a non-oxidative and heterolytic dealkylation of *p*-chloroanisole has been isolated, as is reported in Part VI; but the dealkylation of *p*-chlorophenetole, under similar conditions, involved extensive oxidation, and therefore at least a part of this reaction may have taken place by the homolytic mechanisms. It seems certain that the dealkylations of tertiary amines described in this paper are homolytic; but tertiary amines are most likely to use heterolytic mechanisms when one of the alkyl groups has been so substituted that it is stable in its cationic form (*e.g.*, in the cationic fission product, $CH_2{:}NR_2^+$, of a structure such as $R_2N{\cdot}CH_2{\cdot}NR_2$).

However, there is undoubtedly a quantitative difference in the relative facility of the mechanisms available for the dealkylation of ethers on the one hand and tertiary amines on the other; and our theory would re-describe the difference by stating that, as compared with the nitrosoammonium ion, the nitrosoxonium ion has a larger tendency to lose a carbon cation, and a smaller tendency to lose neutral nitric oxide. This does not seem unreasonable on grounds of the relative electronegativities of oxygen and nitrogen. A hydroxonium ion loses a proton more easily than an ammonium ion does; and there may well be a difference in this direction between oxonium ions and ammonium ions with respect to the loss of cations in general. Again, the loss of nitric oxide after the uptake of nitrosonium ion is equivalent to the loss of an electron from the original base; and known ionisation potentials show that it is considerably easier to take an electron out of a tertiary amine than out of an ether.

(7) Experimental.

(7.1) *Mono- and Di-nitration of Dimethylanilines by Nitric Acid in Acetic Acid.*—The dimethylaniline was purified by the acetic anhydride method. Its *o*-, *m*-, and *p*-nitro-derivatives, the picrate, hydrochloride, and chloroplatinate of the *o*-compound, *p*-nitrosodimethylaniline, 2 : 4-dinitrodimethylaniline, tetramethylbenzidine, and 3 : 3'-dinitrotetramethylbenzidine, all products which were either actually encountered, or were suspected, at some time in the course of the investigation, were prepared for comparison by known methods.

The nitration experiments of this series were set up as stated in Section 2·2. The main variable was the proportion of nitric acid. In most cases the reaction was obviously autocatalytic. In some of the experiments the products were separated by chromatographic methods, first, for the purpose of identifying pure substances, and secondly, in combination with nitro-group determination by titration with titanous chloride, for the quantitative determination of the products which could thus be separated. In other experiments, ordinary methods of crystallisation, solvent extraction, and distillation were used for the separation of the products. Several typical experiments are described below.

Dimethylaniline (5 g.) in solution in acetic acid (30 g.) was nitrated at room temperature during 24 hours with 70% (by wt.) nitric acid (1 mol.). The mixture was diluted with water to 250 c.c., and the precipitate was collected. The filtrate was neutralised with concentrated aqueous ammonia, and extracted continuously with benzene. The precipitate was dissolved in benzene, and the benzene solutions were combined, dried (K_2CO_3), and passed through a column, 30 cm. × 1·5 cm., of activated alumina. In order, the bands were violet (narrow), green (moderate width), yellow (wide), and orange (wide), the last two bands merging slightly. After mechanical division of the column, the violet material was collected in hot alcohol, but there was too little of it for identification; and the green substance was extracted with a mixture of ether and ethyl alcohol, and shown to be *p*-nitrosodimethylaniline (m. p. and mixed m. p. 86—87°). The yellow material was impure *p*-nitrodimethylaniline, but the pure substance (m. p. and mixed m. p. 162—163°) was obtained from it by crystallisation from ethyl alcohol. The orange substance was *o*-nitrodimethylaniline, which was extracted from the adsorbent with hot ethyl alcohol, and identified as its chloroplatinate (m. p. and mixed m. p. 195—196°).

The products of other nitrations with 1 mol. of nitric acid were separated by solvent extraction, distillation, and crystallisation, rather than by chromatography. In this way unconverted dimethylaniline was recovered; and its *o*- and *p*-nitro-derivatives also were obtained.

Experiments with 1·2 mols. of nitric acid led to the detection of *p*-nitrosodimethylaniline, and the isolation of *o*- and *p*-nitrodimethylaniline and of a red substance. In the chromatographic separation, this red substance appeared as a band below the *p*-nitrodimethylaniline band. It tended to crystallise with *p*-nitrodimethylaniline from the crude nitration product, and it could be separated from *p*-nitrodimethylaniline by repeated crystallisation from ethyl alcohol. It had m. p. 195°, and appeared to be a previously unknown *dinitrotetramethylbenzidine* (Found: C, 57·9; H, 5·6; N, 17·2. $C_{16}H_{18}O_4N_4$ requires C, 58·2; H, 5·6; N, 17·0%).

Experiments with 1·4 mols. of nitric acid gave no unchanged dimethylaniline and no nitroso-compound. In some cases very small amounts of a red compound, probably that described above, were seen in the chromatogram. In all cases the main products were *o*- and *p*-nitrodimethylaniline and 2 : 4-dinitrodimethylaniline. In the chromatogram, obtained by passing a benzene solution of the total product through alumina, the *p*-nitro- and the 2 : 4-dinitro-compound together formed a yellow band at the top. The *o*-nitro-compound was deposited as an orange band at the bottom, and the red compound, if present, formed a narrow band between the other bands. The bands were eluted with hot ethyl alcohol. The *p*-nitro-compound, m. p. and mixed m. p. 161—163°, and the 2 : 4-dinitro-compound, m. p. and mixed m. p. 85—86°, were separated by crystallisation from benzene, the former being the less soluble. The *o*-nitro-compound was precipitated from alcoholic solution as its picrate, m. p. and mixed m. p. 101—103°.

Dimethylaniline (2·5 g.) was nitrated with 70% (by wt.) nitric acid (1·4 mols.) in acetic acid (25 g.) at room temperature for 24 hours. Water (100 c.c.) and carbon tetrachloride (40 c.c.) were added, and the whole was shaken for 1 hour and filtered. The precipitate was washed with a small amount of carbon tetrachloride, dried, and weighed. This product was pure *p*-nitrodimethylaniline. The filtrate was neutralised and thoroughly extracted with carbon tetrachloride. The extract was dried (Na_2SO_4), and the solvent was removed by distillation through a short column. The residue was made up to 250 c.c. with benzene, and portions of 50 c.c. of this solution were passed through a column of alumina, benzene containing a little ethyl alcohol being used for the development of the chromatogram. The adsorbed

material of the orange band was known to consist of *o*-nitrodimethylaniline only, and this was extracted with alcohol and estimated by titration with titanous chloride, and back-titration with ferric alum, in the usual way. The yellow band was eluted with alcohol, and the extract was concentrated and poured into water. The product was dried and separated by crystallisation from benzene into fractions consisting of pure *p*-nitrodimethylaniline, pure 2 : 4-dinitrodimethylaniline, and unseparated material. The total yields were as follows: *p*-, 34%; *o*-, 23%; 2 : 4-, 14%.

The experiment next to be described was conducted like the last (but on twice the scale) up to the stage at which the carbon tetrachloride solution was concentrated. The residue was then distilled non-ebulliently at a pressure of about 1 mm. in a special still of small hold-up, the receiving unit of which was cooled at −80°. The yield of the *o*-nitrodimethylaniline (identified through its salts) thus obtained was 25%. The residue from the distillation was collected in alcohol, and the solution was concentrated and poured into water. The precipitate was collected, dried, and crystallised from benzene. In this way a small amount of *p*-nitrodimethylaniline, additional to that which crystallised initially, was isolated, making the total yield 38%. The main part of the material in the benzene solution was obtained, after concentration, as 2 : 4-dinitrodimethylaniline, in a yield of 11%.

An experiment was conducted like the one last described, except that no carbon tetrachloride was used. Instead, the acetic acid solution was cooled at 0°, and the main part of the yield of *p*-nitrodimethylaniline was collected and washed with acetic acid. The acetic acid solution was then distilled under reduced pressure. After all the solvent had been removed, the *o*-nitrodimethylaniline was distilled non-ebulliently as before, with a bath-temperature of about 110°. The residue from the distillation was washed as before, with similar results. The total yields of pure products were as follows: *p*-, 39%; *o*-, 25%; 2 : 4-, 11%.

p-Nitrodimethylaniline on treatment with 70% (by wt.) nitric acid (1 mol.) in acetic acid under similar conditions was converted practically quantitatively into 2 : 4-dinitrodimethylaniline. *o*-Nitrodimethylaniline after similar treatment was recovered practically quantitatively.

(7.2) *Preparation of Substances involved in the Nitration of 2 : 4-Dinitrodimethylanilins to N : 2 : 4 : 6-Tetranitromethylaniline.*—2 : 4-Dinitrodimethylaniline, m. p. 86°, was prepared in quantitative yield by adding aqueous dimethylamine to an alcoholic solution of chloro-2 : 4-dinitrobenzene. 2 : 4-Dinitromethylaniline, m. p. 177°, was obtained in quantitative yield by adding alcoholic methylamine to alcoholic chloro-2 : 4-dinitrobenzene. 2 : 4 : 6-Trinitrodimethylaniline, m. p. 139°, was obtained quantitatively from picryl chloride and dimethylamine, but it is necessary to add the alcoholic solution of picryl chloride to an excess of dimethylamine in aqueous alcohol; for with the reverse order of addition there was obtained a molecular compound of picryl chloride and the required tertiary amine. 2 : 4 : 6-Trinitromethylaniline, m. p. 114°, was prepared in quantitative yield by adding an alcoholic solution of methylamine to one of picryl chloride.

N-Nitroso-2 : 4-dinitromethylaniline was prepared by passing the oxides of nitrogen, generated by the action of nitric acid on arsenious oxide, into the suspension obtained by quickly cooling a hot solution of 2 : 4-dinitromethylaniline in acetic acid (cf. Bamberger and Müllbr, *Ber.*, 1900, **33**, 377). The green solution was poured into water, and the nitrosamine, thus obtained in theoretical yield, was collected and crystallised from ethyl alcohol. It had m. p. 84—85° (Found: C, 37·2; H, 2·6; N, 24·4. Calc.: C, 37·2; H, 2·7; N, 24·6%). *N*-Nitroso-2 : 4 : 6-trinitromethylaniline, similarly prepared from 2 : 4 : 6-trinitromethylaniline, had m. p. 106° (Found: C, 31·3; H, 2·0. Calc.: C, 31·0; H, 1·9%).

N : 2 : 4-Trinitromethylaniline was prepared by two methods. (*a*). 2 : 4-Dinitroaniline was first *N*-nitrated, and then the product was methylated. The finely powdered amine (50 g.) and acetic anhydride (80 c.c.) were together slowly added at 25—30° to the mixture of nitric acid (100 c.c.), acetic acid (80 c.c.), and acetic anhydride (15 c.c.). Stirring was continued for 48 hours at room temperature, and, most of the original amine having by that time dissolved, the mixture was poured on ice. The yellow precipitate was collected, and extracted with saturated aqueous sodium carbonate. The filtrate was extracted with chloroform, and the chloroform solution was then extracted with aqueous sodium carbonate. The combined sodium carbonate solutions were acidified, and the precipitated nitroamine was collected and crystallised from ethyl alcohol. The pure product had m. p. 79°, and weighed 17 g. (Found: C, 31·9; H, 1·8. Calc.: C, 31·6; H, 1·8%). A solution of this nitramine (11 g.) in methyl alcohol (35 c.c.) was treated with a solution of sodium methoxide, prepared from sodium (1·7 g.) and methyl alcohol (35 c.c.), and then with methyl iodide (10 c.c.). After 4 days, the solution was boiled for 3 hours, and then concentrated and poured into aqueous sodium carbonate. The precipitated product (3 g.) was collected and crystallised from ethyl alcohol. It had m. p. 113—114° (Found: C, 34·9; H, 2·8. Calc.: C, 34·7; H, 2·5%). (*b*) *N* : 2 : 4-Trinitromethylaniline was obtained almost quantitatively by the interaction of dinitrogen pentoxide and 2 : 4-dinitromethylaniline. The dinitrogen pentoxide (5 g.), prepared as described in another communication (*J.*, 1950, 2452), and dissolved in chloroform (100 g.), was added to a suspension of the amine (8 g.) in chloroform (30 g.). The amine slowly dissolved, and a pale yellow solid separated. After extraction with water to remove nitric acid, the precipitated nitroamine was collected. A further quantity was obtained by concentrating the chloroform solution. The product (10 g.), crystallised from alcohol, had m. p. 113—114°.

(7.3) *Percentage Conversions of Different Substances into N : 2 : 4 : 6-Tetranitromethylaniline.*—The seven compounds whose preparation has just been described were each nitrated to give *N* : 2 : 4 : 6-tetranitromethylaniline under a fixed set of conditions; and the yields were compared. The composition of the nitration solution used in these experiments was closely controlled; to within ±0·1% it was as follows: H_2SO_4, 51·8; HNO_3, 25·8; H_2O, 22·3; HNO_3, 0·1% by weight. The determination of nitrous acid in nitration media is described in an accompanying paper (*J.*, 1950, 2400).

A weighed quantity (*ca.* 2 g.) of the compound to be nitrated was added to the nitrating solution (38·6 g.). After 7 days the product was poured into water (250 c.c.), and the *N* : 2 : 4 : 6-tetranitro-

methylaniline was collected in a sintered-glass crucible, washed with cold water, and dried to constant weight in a desiccator over sulphuric acid (Found: C, 29·5; H, 2·3; N, 24·1. Calc.: C, 29·3; H, 1·8; N, 24·4%).

The yield thus measured was corrected for the solubility of the product. The correction was determined by adding a weighed amount (*ca.* 2 g.) of carefully purified *N* : 2 : 4 : 6-tetranitromethylaniline to the nitrating mixture (38·6 g.), pouring the whole into water (250 c.c.), and recovering the original substance as described. The correction thus determined amounted to about 1%. It was slightly dependent on the amount of substance being determined; this small effect was also measured and the appropriate allowances were made.

Next a correction was applied for the impurities in the weighed yield, on the basis of the m. p. (clearing point) of the sample. It was necessary to know approximately the m. p. of pure *N* : 2 : 4 : 6-tetranitromethylaniline, and the cryoscopic constant of the substance. The highest m. p. observed under the conditions of our measurements was 129·3°. The sample having this m. p. had been subjected to a long series of fractional crystallisations from benzene and from ethyl alcohol, with intercalated fractional adsorptions on activated alumina. We took this as the m. p. of the pure substance. Our value for the cryoscopic constant was 19 deg. g.-mol.$^{-1}$ kg. This was determined by adding to the purified fused substance known weights, up to 3%, of *N* : 2 : 4-trinitromethylaniline and repeating the determination of the m. p.

The results obtained in this series of experiments have been given in Section 4.1. Additional experiments were carried out (*a*) in the presence of urea nitrate, (*b*) in the presence of several times more nitrous acid than was present in the experiments of the main series. These changes of conditions appeared to make but little difference to the results.

(7.4) *Nitration of* 2 : 4-*Dinitrodimethylaniline in Aqueous Nitric Acid.*—The amine (1 g.) was dissolved at room temperature in a mixture of absolute nitric acid (8 c.c.) and water (12 c.c.). Nitrogen dioxide was evolved, and an orange solid separated. After 24 hours the mixture was poured into water. The precipitated product, once crystallised from acetic acid, had m. p. 174°. The mixed m. p. with 2 : 4-dinitromethylaniline was 175—176°.

The product from a similar experiment made with a mixture of 10 c.c. each of nitric acid and water, was triturated with successive portions of ether, use of this solvent being suggested by preliminary experiments on the solubilities in various solvents of all the substances whose preparation is described in Section 7.2. After 7 such treatments, pure 2 : 4-dinitromethylaniline remained, m. p. and mixed m. p. 176°. The residue obtained on evaporation of the ether had m. p. *ca.* 95° with previous softening. After crystallisation from alcohol, it was found to be *N*-nitroso-2 : 4 : 6-trinitromethylaniline, m. p. and mixed m. p. 105°.

The original amine (1 g.) was dissolved in a mixture of nitric acid (7 c.c.) and water (3 c.c.). The solution became green and then purple, nitrogen dioxide being evolved. After 24 hours, the solution was poured into water. The product, crystallised once from alcohol, proved to be *N*-nitroso-2 : 4 : 6-trinitromethylaniline, m. p. and mixed m. p. 106°.

A similar experiment with 10 c.c. of 98% nitric acid gave a precipitated product of m. p. 126°, which was identified as *N* : 2 : 4 : 6-tetranitromethylaniline by the mixed m. p., 127°.

(7.5) *Nitration of* 2 : 4-*Dinitromethylaniline and of its* N-*Nitro-derivative in Aqueous Nitric Acid.*—2 : 4-Dinitromethylaniline (0·5 g.) was dissolved in 10 c.c. of 70% nitric acid. After 2 hours, the brownish-purple solution was poured into water. The product, *N* : 2 : 4-trinitromethylaniline, after crystallisation from ethyl alcohol, was identified by its m. p., 111°, and mixed m. p., 112—113°.

An experiment was started in the same way, but the nitration mixture was kept for 10 days before being poured into water. The product was then *N* : 2 : 4 : 6-tetranitromethylaniline, as was shown by its m. p. and mixed m. p. When the amine used in this experiment was replaced by *N* : 2 : 4-trinitromethylaniline in a parallel experiment, the product was the same.

2 : 4-Dinitromethylaniline (0·5 g.) was nitrated at room temperature with 70% aqueous nitric acid to which sodium nitrite (0·36 g., 2 mols.) had been added. After 5 hours, the solution was poured into water, and the solid product crystallised from alcohol. It had m. p. 106°, and was identified by mixed m. p. with *N*-nitroso-2 : 4 : 6-trinitromethylaniline.

(7.6) *Nitration of* 2 : 4-*Dinitrodimethylaniline by Nitric Acid in Aqueous Sulphuric Acid.*—The general results of these experiments have been summarised in Section 4.4, and only a few notes on the separations need be added. All the nitrations were allowed 24 hours at the room temperature, and the solutions were then poured into water, and the products were collected. The product from the experiments with "50%" aqueous sulphuric acid and 2 mols. of nitric acid, after crystallisation from acetic acid, had m. p. 175°, and the same mixed m. p. with 2 : 4-dinitromethylaniline. The products from the experiments with the same aqueous sulphuric acid and 5—10 mols. of nitric acid had m. p.s about 90° with previous softening, and had to be triturated with ether, and crystallised from ethyl alcohol, before pure *N*-nitroso-2 : 4 : 6-trinitromethylaniline, m. p. and mixed m. p. 106°, was obtained. For dealing with the products of the long series of experiments made with "55—85%" aqueous sulphuric acid and 2—10 mols. of nitric acid, a combination of trituration with ether and chromatography on alumina was employed. The treatment with ether nearly always left a residue of *N* : 2 : 4 : 6-tetranitromethylaniline, which was identified by its m. p. and mixed m. p., if necessary after crystallisation from alcohol. The material dissolved by the ether was recovered by evaporation, dissolved in benzene, and adsorbed on a column of activated alumina. The usual result was the production of a very narrow orange band high in the column, and, considerably lower down, a large orange-yellow band with a pale yellow fringe at the bottom. The material in the very narrow orange band was not identified. The substance responsible for the large orange-yellow band was in all cases 2 : 4-dinitrodimethylaniline, and,

after extraction with alcohol, and crystallisation from light petroleum containing benzene, was identified by its m. p. and mixed m. p. The material in the pale yellow fringe appeared to contain *N* : 2 : 4 : 6-tetranitromethylaniline, though this was not obtained from it sufficiently pure for satisfactory identification. The experiments with " 95% " aqueous sulphuric acid and 1·25—3·0 mols. of nitric acid gave products, which were dissolved in benzene, and then adsorbed on alumina. The chromatograms consisted of an orange band above, and a yellow band below, the yellow band becoming larger and the orange band smaller when the proportion of nitric acid was increased. The material, extracted from the yellow band with hot ethyl alcohol, was identified by its m. p., 138°, and mixed m. p. as 2 : 4 : 6-trinitrodimethylaniline. The material, similarly obtained from the orange-yellow band, was identified by m. p. and mixed m. p. as 2 : 4-dinitrodimethylaniline. Experiments with " 95% " sulphuric acid and 4—5 mols. of nitric acid were carried out, but it was not found possible satisfactorily to separate and identify the products. Experiments with 10 mols. of nitric acid gave nearly pure *N* : 2 : 4 : 6-tetranitromethylaniline.

A series of experiments were conducted in which urea nitrate was employed in place of nitric acid. In " 70% " aqueous sulphuric acid with 1·25—5·0 mols. of urea nitrate, no reaction took place, the original amine being quantitatively recovered. In " 95% " aqueous sulphuric acid with 1·25—3·0 mols. of urea nitrate, the products behaved like those obtained by the use of corresponding amounts of nitric acid; and they were separated by the same methods into the same substances.

(7.7) *Nitration of 2 : 4-Dinitromethylaniline and of its N-Nitroso- and N-Nitro-derivatives by Nitric Acid in Aqueous Sulphuric Acid.*—These experiments have been described in Section 4.5, and only a few notes need be added. The nitrosoamine, or other initial substance (0·5 g.), was added to a mixture of " 70% " aqueous sulphuric acid (7·5 c.c.) and nitric acid (2·5 c.c.) at room temperature. The orange-yellow substance, isolated by pouring the solution into water at a very early stage of the reaction, was crystallised from acetic acid, and identified as 2 : 4-dinitromethylaniline by its m. p., 174—175°, and mixed m. p. The pale yellow substance isolated by stopping the nitration at a somewhat later stage, was crystallised from ethyl alcohol, and was then identified as *N* : 2 : 4-trinitromethylaniline by its m. p., 111—113°, and mixed m. p. The final product, *N* : 2 : 4 : 6-tetranitromethylaniline, was identified as usual by m. p. and mixed m. p.

Attempts were made to convert *N*-nitroso-2 : 4-dinitromethylaniline into *N*-2 : 4-trinitromethylaniline by oxidation with hydrogen peroxide. A solution of the nitrosoamine (1 g.) in acetic acid (10 c.c.) was treated with 30% aqueous hydrogen peroxide (1 c.c.). A vigorous reaction set in and yellow crystals, consisting of 2 : 4-dinitromethylaniline, separated. Their m. p., and the mixed m. p., were both 174—175°. Hydrogen peroxide in pyridine had no action on the nitrosoamine. Hydrogen peroxide in an aqueous borate buffer, pH 7—8, had no action in the cold; but on heating decomposition took place, the product being again 2 : 4-dinitromethylaniline. An aqueous solution of Caro's acid, made slightly alkaline with sodium carbonate, also had no action in the cold, but heating produced 2 : 4-dinitromethylaniline.

Attempts were made to isomerise *N*-nitroso-2 : 4-dinitromethylaniline by the use of acids. The nitrosoamine (4 g.) was left in contact with concentrated hydrochloric acid (45 c.c.) for 30 minutes at room temperature. The solid, without dissolving, became bright orange-yellow. After dilution with water, it was collected, crystallised from acetic acid, and found to be 2 : 4-dinitromethylaniline, m. p. and mixed m. p. 174—175°. The same substance was produced when dry hydrogen chloride was passed into a suspension of the nitrosamine in ether. It was also produced by treating the nitrosoamine (1 g.) with nitric acid (1 g.) in acetic acid (10 g.), with 70% aqueous nitric acid (10 g.), or with a mixture of sulphuric acid (10 g.) and acetic acid (10 g.). It was identified by m. p. and mixed m. p. in all cases.

The reaction of the nitrosamine (1 g.) with hydrogen chloride in ether was repeated in the presence of dimethylaniline (1·5 g.). A white precipitate appeared, which redissolved, an orange precipitate taking its place. This was collected, and shaken with ether and aqueous sodium carbonate. The undissolved solid was crystallised from acetic acid, and identified by its m. p., 174—175°, and mixed m. p. as 2 : 4-dinitromethylaniline. The green ethereal solution was dried and evaporated. The solid residue was crystallised from light petroleum and identified by its m. p., 80°, and mixed m. p. as *p*-nitrosodimethylaniline.

(7.8) *Interconversion of 2 : 4 : 6-Trinitrodimethylaniline, 2 : 4 : 6-Trinitromethylaniline, N-Nitroso-2 : 4 : 6-trinitromethylaniline, and N : 2 : 4 : 6-Tetranitromethylaniline.*—2 : 4 : 6-Trinitrodimethylaniline (1 g.) was dissolved in " 70% " aqueous sulphuric acid (30 c.c.) containing 2 mols. of nitric acid. After 24 hours at room temperature, the solution was poured into water, and the product was collected, dried, and triturated with ether. The undissolved portion was crystallised from alcohol, and identified as *N* : 2 : 4 : 6-tetranitromethylaniline by m. p. and mixed m. p. The material which dissolved in the ether was recovered and purified by chromatography from benzene solution with alumina as adsorbent. The large orange band, eluted with alcohol, yielded 2 : 4 : 6-trinitromethylaniline, which, after crystallisation from alcohol, was identified by its m. p., 112°, and mixed m. p. A similar experiment with 10 mols. of nitric acid yielded *N* : 2 : 4 : 6-tetranitromethylaniline only.

2 : 4 : 6-Trinitromethylaniline (0·5 g.) was added to " 70% " aqueous sulphuric acid (10 c.c.) containing 10 mols. of nitric acid. The colour of the solution became steadily paler; and, after 2 hours, the product was isolated by adding water, and identified as *N* : 2 : 4 : 6-tetranitromethylaniline. The same conversion was carried out by using aqueous nitric acid of various concentrations between 60% and 90%.

2 : 4 : 6-Trinitrodimethylaniline (0·5 g.) was dissolved in 70% aqueous nitric acid (10 c.c.) at room temperature. Nitrogen dioxide was evolved. After 24 hours the solution was poured into water, and the product was collected and crystallised from alcohol. It had m. p. 106°, and was identified by mixed m. p. as *N*-nitroso-2 : 4 : 6-trinitromethylaniline.

2 : 4 : 6-Trinitromethylaniline (0·5 g.) was dissolved in 70% aqueous nitric acid (10 c.c.) to which sodium nitrite (0·28 g., 2 mols.) had been added. After 1 hour, the product was isolated, and identified as *N*-nitroso-2 : 4 : 6-trinitromethylaniline, as in the preceding experiment.

N-Nitroso-2 : 4 : 6-trinitromethylaniline (0·5 g.) was added to a mixture of " 70% " aqueous sulphuric acid (8 c.c.) and nitric acid (2 c.c.). The solid, without dissolving, soon became colourless. After dilution with water, the crystalline substance was collected and identified as *N* : 2 : 4 : 6-tetranitromethylaniline by m. p. and mixed m. p.

(7.9) *Dealkylation of* 2 : 4-*Dinitro- and* 2 : 4 : 6-*Trinitro-dialkylanilines.*—Some of the experiments mentioned in this Section were carried out with higher homologues, containing ethyl or n-butyl groups in place of the methyl groups of the methyl- and dimethyl-aniline derivatives employed for the rest of the work described in this paper. These homologues were prepared, either as initial material for experiments, or for the identification of products by comparison, by using methods quite analogous to those employed for the preparation of the methyl compounds (Section 7.2). The 2 : 4-dinitrodiethylaniline had m. p. 80°, the 2 : 4-dinitroethylaniline, m. p. 114°, and the *N*-nitroso-2 : 4-dinitroethylaniline, m. p. 56°; but 2 : 4-*dinitro-n-butylaniline* could be obtained only as a liquid. It was prepared by boiling the chlorodinitrobenzene with a 3-fold excess of di-n-butylamine for 5 hours in ethyl alcohol, washing the product several times with aqueous hydrochloric acid, drying it in light petroleum with sodium sulphate, and pumping off the solvent (Found : C, 57·0; H, 7·7. $C_{14}H_{21}O_4N_3$ requires C, 57·0; H, 7·1%).

The effects due to added nitrous acid on the demethylation of 2 : 4-dinitrodimethylaniline by nitric acid in acetic acid, and on the analogous reaction of 2 : 4 : 6-trinitrodimethylaniline as effected by nitric acid in sulphuric acid, have been noted in Section 5.1. So also has the effect of added water in promoting the demethylating action of nitrous acid on 2 : 4-dinitrodimethylaniline, and on 2 : 4-dinitrodiethylaniline, in solution in sulphuric acid. Some further details will be given here concerning dealkylations effected by dinitrogen tetroxide, by dilute nitric acid containing nitrous acid, by chromic acid, and by permanganic acid.

2 : 4-Dinitrodimethylaniline, in solution in chloroform, was treated with a solution of freshly distilled dinitrogen tetroxide in the same solvent. The solution became green, and an energetic reaction set in. When reaction had abated, methyl alcohol was added, and the solution concentrated by evaporation. The yellow crystalline substance which separated was collected, and, after crystallisation from ethyl alcohol, was identified by its m. p. and mixed m. p. as 2 : 4-dinitromethylaniline. A similar experiment was made with 2 : 4-dinitrodiethylaniline. The similarly isolated product had m. p. 113—114°, and was identified by comparison and mixed m. p. as 2 : 4-dinitroethylaniline.

2 : 4-Dinitrodimethylaniline in solution in acetic acid was treated with a solution of dinitrogen tetroxide in that solvent. Again there was a vigorous reaction. After reaction had subsided, methyl alcohol was added, and then water. The precipitated product was identified by its m. p. and mixed m. p. as *N*-nitroso-2 : 4-dinitromethylaniline. A similar experiment was made with 2 : 4-dinitrodiethylaniline. The product, m. p. 55°, was identified by mixed m. p. as *N*-nitroso-2 : 4-dinitroethylaniline.

Experiments like the two just described on 2 : 4-dinitrodimethylaniline were carried out with 2 : 4-dinitromethylaniline. When chloroform was the solvent this amine was recovered unaltered, but when acetic acid was employed the product was *N*-nitroso-2 : 4-dinitromethylaniline. A similar experiment with 2 : 4-dinitroethylaniline likewise gave the unaltered secondary amine when chloroform was the solvent, but its *N*-nitroso-derivative when the solvent was acetic acid.

In the experiments with 2 : 4-dinitrodimethyl- and 2 : 4-dinitrodiethyl-aniline, nitric oxide was copiously evolved. In an experiment with 2 : 4-dinitrodimethylaniline, chloroform being the solvent, the chloroform solution obtained at the conclusion of the reaction was shaken with water; the aqueous solution thus obtained gave the reactions of formaldehyde. In an experiment with 2 : 4-dinitrodiethylaniline, acetic acid being the solvent, the evolved gases were passed through water; the aqueous solution thus prepared gave the reactions of acetaldehyde.

In some experiments with dilute nitric acid containing nitrous acid as the dealkylating agent attention was directed mainly to the recovery of the compound formed from the eliminated alkyl group. 2 : 4-Dinitrodimethylaniline, 2 : 4-dinitrodiethylaniline, or 2 : 4-dinitrodi-n-butylaniline (10 g. of any one) was warmed with 20% aqueous nitric acid (200 c.c.) containing nitrous acid, and a current of air was passed through the solution. The gases thus carried off were passed through a 10% solution of 2 : 4-dinitrophenylhydrazine (50 c.c.) in hydrochloric acid. A copious precipitation occurred of the 2 : 4-dinitrophenylhydrazone of formaldehyde, acetaldehyde, or n-butaldehyde. These compounds, having m. p.s 155°, 147°, and 123°, respectively, were identified by mixed m. p.s with authentic specimens. A blank experiment was conducted in which n-butyl alcohol was used in place of 2 : 4-dinitrodi-n-butylaniline. In this case no precipitate was formed in the 2 : 4-dinitrophenylhydrazine trap; and extraction of the aqueous solution with ether yielded n-butyl nitrite, b. p. 74—76°, identified by its physical properties and reactions.

2 : 4-Dinitrodiethylaniline (1 g.), dissolved in " 30% " aqueous sulphuric acid (20 c.c.), was treated with chromium trioxide (2 g.). The mixture immediately became green, and acetaldehyde could be aspirated from the solution. After 10 minutes at room temperature, the solution was poured into water, and the precipitated product was collected, and, after crystallisation from alcohol, was identified by m. p. and mixed m. p. as 2 : 4-dinitroaniline.

A similar experiment was made with acetic acid as the solvent instead of aqueous sulphuric acid. In this case reaction was induced by warming the mixture. When, after 1 hour, the solution was poured into water, a strong odour of acetaldehyde was noticed, and a crystalline product was precipitated. This was crystallised from ethyl alcohol, and identified by m. p. and mixed m. p. as 2 : 4-dinitroethylaniline.

A solution of 2 : 4-dinitrodimethylaniline (1·0 g.) in " 30% " aqueous sulphuric acid (40 c.c.) was treated with potassium permanganate (1 g.). A gas was evolved, which was shown to contain formaldehyde, and a yellow precipitate was formed. Water was added, and the precipitate was collected. This product, after crystallisation from ethyl alcohol, was identified by m. p. and mixed m. p. as 2 : 4-dinitromethylaniline.

A solution of 2 : 4-dinitrodiethylaniline (1 g.) in " 30% " aqueous sulphuric acid (40 c.c.) was treated with potassium permanganate (2 g.). A vigorous reaction ensued, and a gas was evolved, which contained acetaldehyde. Water was added, and the precipitated product was collected. It was crystallised from ethyl alcohol, and identified by m. p. and mixed m. p. as 2 : 4-dinitroaniline.

Note.—Details of some further experiments relevant to the subject matter of this paper are included in Part VIII.

UNIVERSITY COLLEGE OF NORTH WALES, BANGOR.
WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1.

[*Received, December 17th*, 1949.]

---

514. *Kinetics and Mechanism of Aromatic Nitration. Part VIII. The Rearrangement of Aromatic N-Nitroamines.*

By E. D. HUGHES and G. T. JONES.

A study of the proportions in which nitro-products are formed in the acid-catalysed rearrangement of phenylnitramine, and in the nitration of aniline with nitric acid under comparable conditions, has shown that two very different types of orientation are involved in the two reactions.

The formation of nitric acid, or of any other nitrating agent, was not observed during the rearrangement of *p*-nitrophenylmethylnitroamine under a variety of conditions. The product was invariably 2 : 4-dinitromethylaniline, and the transfer of the nitro-group to a " foreign " aromatic nucleus could not be established.

In the case of 2 : 4-dinitrophenylmethylnitramine, acidolysis of the nitro-group was shown to occur under conditions conducive to the rearrangement; and transfer of the nitro-group to a " foreign " aromatic compound was effected. It was demonstrated, however, that nitric acid, in the amount that could be produced by acidolysis, is not capable of converting the denitration product, 2 : 4-dinitromethylaniline, into the rearrangement product, 2 : 4 : 6-trinitromethylaniline, nearly as smoothly or as readily as the latter is formed by rearrangement under comparable conditions.

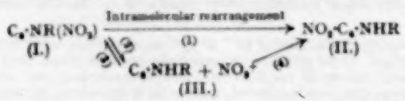
The evidence as a whole may be consistently interpreted on the basis of a predominating intramolecular mechanism for the nitramine rearrangement.

(1) *Background, Object, and Methods.*

(1.1) *Aim of this Work.*—The motive for undertaking this work arose in connexion with the investigation described in the preceding paper, where use has already been made of the conclusion which will be reached.

The hypothesis that aromatic primary and secondary amines, in so far as they are nitrated in the form of free amines rather than as salts, normally undergo " indirect " nuclear nitration, an *N*-nitration being followed by the intramolecular migration of the nitro-group, was advanced more than 50 years ago but has never definitely been proved or disproved. The problem of the mechanism of the rearrangement of aromatic nitramines, especially the question of whether the nitro-group is internally transferred, or whether it separates to form a nitrating agent which subsequently attacks the aromatic nucleus, has been under consideration for a similar length of time, but again no unequivocal conclusion has been reached. These two questions are obviously linked together, and they will be considered together in this paper.

(1.2) *Methods.*—The matter to be decided may be stated, and the methods by which it might be settled may be seen, with the aid of the scheme written below:



Here, C_6 represents the benzene ring without restriction as to the substituents which it may be carrying in addition to those expressed in the formulæ, and NO_2^+ means either the free nitronium ion, or some nitronium-ion carrier or source, such as its hydrate, the nitric acidium ion, or even nitric acid.

The problem is to determine whether the conversion of the *N*-nitro-compound (I) into the *C*-nitro-compound (II) follows the internal route (1), or whether it takes the external route (2 + 4) by way of the intermediates (III). There are three obvious ways in which one might seek evidence on this question. One might try to compare, using identical conditions of solvent and temperature, (*a*) the orientation of substitution in processes (1) and (4), (*b*) the rates of destruction of (I) in processes (1) and (2), (*c*) the rates of formation of (II) in processes (1) and (4). Comparison (*a*) must be quantitative, if it is to have any real value. Comparisons (*b*) and (*c*) may be made initially in a qualitative manner, in case gross rate differences are involved; and they may be carried to a quantitative stage, if the results should render that necessary. Comparison (*b*) might be defeated by reaction (3), unless precautions to prevent this are taken; and the simplest precaution is to operate in the presence of some substance which will react with one of the products (III) as fast as it is formed (the convenient one being the nitronium ion or its carrier), thus inhibiting reaction (3). The object of comparisons (*a*) and (*c*) might be defeated by the observation of identical orientations or rates; for identical orientations might mean either that the reaction assumed to be (1) is really (2 + 4), or that the reaction assumed to be (4) is really (3 + 1); and identical rates might mean either of these eventualities, with the added condition that stages (2) and (3) are fast; and so, in either case, the experimental indication would be ambiguous. The observation of a marked difference of orientation, or of rate, would, however, point to a definite conclusion.

In the present study we have used all three methods, (*a*), (*b*), and (*c*); and all point to the same conclusion.

(1.3) *Previous Work.*—It was shown by Bamberger that phenylnitramine, phenylmethylnitramine, and similar nitramines, undergo rearrangement on treatment with aqueous strong acids, or with hydrogen chloride in organic solvents, to yield mainly *o*-nitroaniline or its derivatives, and, in smaller amounts, *p*-nitroaniline or its derivatives (*Ber.*, 1893, **26**, 471, 485; 1894, **27**, 359). Having found, in a parallel series of researches, that treatment of primary and secondary aromatic amines by non-acidic nitrating agents, such as dinitrogen pentoxide, often leads to *N*-nitration, he made the suggestion that the nuclear nitration of these bases by acidic nitrating agents in general proceeds by *N*-nitration with subsequent rearrangement (*Ber.*, 1894, **27**, 584; 1895, **28**, 399; Bamberger and Hofl, *Ber.*, 1897, **30**, 1248; *Annalen*, 1900, **311**, 91).

Holleman, Hartogs, and Linden (*Ber.*, 1911, **44**, 704) attempted to test Bamberger's hypothesis by a somewhat incomplete application of the above-mentioned method (*a*) to the rearrangement of phenylnitramine and the nitration of aniline. For each of these processes they measured the proportions of *o*-, *m*-, and *p*-nitro-products by the technique of thermal analysis. They concluded that the nuclear nitration of aniline does not always proceed by way of an initial *N*-nitration. The following results are typical of those which led to this deduction:

Process.	Conditions.	*o*-, %.	*m*-, %.	*p*-, %.
Nitration	$Ph{\cdot}NH_2NO_2$ in 95% aq. H_2SO_4 at −20°	4	39	56
,,	$Ph{\cdot}NH_2NO_2$ in 80% aq. HNO_3	5	32	62
,,	$Ph{\cdot}NH_2NO_2$ in Ac_2O	82·1	2·9	15·0
Rearrangement	74% aq. H_2SO_4 at −20°	95	1·5	3·5

Considering these figures, the inference drawn does seem an extremely reasonable one. The demonstration is not, however, conclusive, because the conditions of nitration and of rearrangement were not the same. It is a commonplace that the proportions in which nitro-compounds are formed in the nitration of bases are sensitive to the conditions, and it is not established that the proportions in which they are produced by rearrangement do not also vary with the conditions.

A general investigation of the rearrangement of nitramines was conducted by Orton and his co-workers (*J.*, 1902, **81**, 490, 806; 1905, **87**, 389; 1907, **91**, 146; 1908, **93**, 725; *Rep. Brit. Assoc.*, 1912, 117; Bradfield and Orton, *J.*, 1929, 915). They noted that the reaction is subject to general acid catalysis. Their main conclusion was that, although in special cases nitramines in acid solution could be observed to nitrate a foreign aromatic compound, thus proving that a nitrating agent is present in these conditions, " no nitrating agent invariably and normally appears in the system in which a nitramine is undergoing isomeric change." Orton made it clear that the case is very different from that of the acid-catalysed rearrangement of chloramines in polar solvents, for which he always found it possible to prove the production of free chlorine. However, he regarded the conclusion quoted above as requiring further definition and elucidation, such as it is the purpose of this paper to provide.

(2) *Observations on the Rearrangement of Aromatic Nitramines.*

(2.1) *Orientation in the Rearrangement of Phenylnitramine and in the Nitration of Aniline.* The experiments to be reported in this Section extend those of Holleman, Hartogs, and Linden (*loc. cit.*), the present object being to compare the proportions in which nitro-products are formed in the rearrangement of phenylnitramine, and in the nitration of aniline, under the same conditions. If, in a given medium, phenylnitramine is rearranged by route (2 + 4), *i.e.*, as the result of an initial acidolysis to aniline and nitric acid, then one equivalent of nitric acid is made available for the second stage of the reaction, namely, the nuclear nitration of the aniline. Accordingly, it was judged that the addition of pure aniline nitrate to the medium would provide the nitration conditions most satisfactory for comparison with the rearrangement of the nitramine. Preliminary experiments were carried out in order to determine favourable common conditions for the smooth occurrence of the two reactions.

It was confirmed that *o*-nitroaniline is the main product of the rearrangement of phenylnitramine in 74% (by weight) aqueous sulphuric acid. However, the addition of aniline nitrate to this acid gave tarry products and unchanged aniline. It was also found that *m*- and *p*-nitroanilines are the main products formed by the addition of aniline nitrate to concentrated sulphuric acid. But the addition of phenylnitramine to the concentrated acid resulted in a violent reaction, in which brown fumes were evolved and tarry products formed. It appears that the rearrangement proceeds more smoothly than the nitration in 74% aqueous sulphuric acid, but that nitration takes place more smoothly than the rearrangement in the anhydrous acid. This in itself indicates that there is no very close relationship between the two processes.

Both reactions take place fairly smoothly, with the formation of mononitroanilines in high yield, and only traces of tar, in sulphuric acid monohydrate, *i.e.*, 84—85% (by weight) aqueous sulphuric acid, maintained just above its freezing point. For these conditions, the proportions of the isomerides in the product of each reaction were determined by thermal analysis, with the following results:

Process.	*o*-, %.	*m*-, %.	*p*-, %.
Rearrangement of phenylnitramine	93	0	7
Nitration of aniline	6	34	59

Clearly, two very different types of orientation are involved in these two reactions.

(2.2) *Internal Nitroxyl Migration* versus *External Nitroxyl Transfer with p-Nitrophenylmethylnitramine.*—Little information appears in the literature concerning the rearrangement of this compound. Its preparation from *p*-nitroaniline was described by Pinnow (*Ber.*, 1897, **30**, 837), and also by Bamberger and his co-workers (*ibid.*, p. 1248), who mention that it is rearranged to 2 : 4-dinitromethylaniline by sulphuric acid in acetic acid at 0°.

We found that th nitramine is rearranged to the 2 : 4-dinitro-compound, instantly by cold concentrated sulphuric acid, rapidly by cold hydrogen chloride in ethyl alcohol or in acetic acid, and slowly by cold ethereal or aqueous hydrogen chloride. The conversion takes place fairly rapidly when the nitramine is boiled with aqueous hydrochloric acid or with formic acid, or when it is heated on the water-bath with a solution of trichloroacetic acid in acetic acid. On the whole, the rearrangement of *p*-nitrophenylmethylnitramine is more facile than is that of 2 : 4-dinitrophenylmethylnitramine, which is discussed below.

No sign of the formation of nitric acid, or of any other nitrating agent, could be discerned during these rearrangements. Attempts were made to detect the formation of a nitrating agent by carrying out the rearrangements in the presence of the reactive aromatic compounds *p*-xylene and phenol. The rearranging agents employed in these experiments were concentrated sulphuric acid, 80% (by weight) aqueous sulphuric acid, and hydrogen chloride in acetic acid. However, the product was always the usual rearrangement product, 2 : 4-dinitromethylaniline. No *p*-nitromethylaniline could be detected, and in no case could any uptake of a nitro-group by the added aromatic compound be established. This absence of denitration during the rearrangement of *p*-nitrophenylmethylnitramine forms another contrast with the reaction of 2 : 4-dinitrophenylmethylnitramine, next to be discussed.

(2.3) *Internal Nitroxyl Migration* versus *External Nitroxyl Transfer with 2 : 4-Dinitrophenylmethylnitramine.*—On the whole, the rearrangement of this nitramine to 2 : 4 : 6-trinitromethylaniline is not a facile process. However, it took place somewhat rapidly in cold concentrated sulphuric acid. In 80% (by weight) aqueous sulphuric acid the rearrangement still proceeded slowly, requiring about 2 hours to become nearly complete at 25°. None of the other reagents which were tried brought about smooth rearrangement. Hydrogen chloride in ether, which was Bamberger's usual rearranging agent, cold concentrated aqueous hydro-

chloric acid, and cold solutions of trichloroacetic acid in either water or acetic acid, had no facile action. Hot aqueous hydrochloric acid, boiling formic acid, fused trichloroacetic acid at 100°, a boiling 30% solution of trichloroacetic acid in water, and a cold mixture of sulphuric and acetic acids (equal volumes) denitrated the side chain, giving 2 : 4-dinitromethylaniline. With hot concentrated nitric acid, and even with 80% (by volume) aqueous nitric acid after a longer period of heating, further nitration occurred, the product being 2 : 4 : 6-trinitrophenylmethylnitramine.

The above-mentioned derivatives show that nitric acid can readily be produced by acidolysis of 2 : 4-dinitrophenylmethylnitramine. We have made experiments to determine whether it is in fact produced under the conditions of the rearrangement, and at a rate comparable to that of rearrangement. Because of the reversibility of the acidolysis of nitramines, the method, as has already been explained, is to conduct the rearrangement in the presence of an aromatic compound which is expected rapidly and irreversibly to take up nitric acid, if this is being formed. As the added (" foreign ") aromatic compound, we have used *p*-xylene, phenol, and dimethylaniline. As rearranging medium, we have employed concentrated sulphuric acid and 80% aqueous sulphuric acid. In order to provide a basis of comparison for the products of these experiments, a parallel series of experiments has been conducted on the nitration of each of the foreign aromatic compounds by nitric acid in the various rearranging media. The method was first to introduce the foreign aromatic compound into the rearranging medium in each of two similar experiments, and then to add to one the 2 : 4-dinitrophenylmethylnitramine, and to the other an equivalent amount of nitric acid. No attempt was made to identify all the reaction products in the more complicated cases, but the most important compounds were isolated and characterised. The results of these experiments are summarised in Table I.

TABLE I.

Products obtained by conducting the rearrangement of 2 : 4-*dinitrophenylmethylnitroamine in acid media in the presence of foreign aromatic compounds. Comparison with the action of nitric acid on the same compounds in the same media.*

Aromatic compound.	Reagent: $C_6H_3(NO_2)_2$·NMe(NO_2). Interaction.	Rearrangement.	Reagent: HNO_3.
Medium : Concentrated sulphuric acid :			
p-$C_6H_4Me_2$	$C_6H_3(NO_2)Me_2$ $C_6H_3(NO_2)_2$·NHMe	—	$C_6H_3(NO_2)_2Me_2$
C_6H_5·OH	—	$C_6H_3(NO_2)_2$·NHMe Polycondensed products	*p*-$C_6H_4(NO_2)$·OH
C_6H_5·NMe_2	—	$C_6H_3(NO_2)_2$·NHMe	*m*-$C_6H_3(NO_2)$·NMe_2 2 : 4-$C_6H_3(NO_2)_2$·NMe_2
Medium : 80% Aqueous sulphuric acid :			
p-$C_6H_4Me_2$	$C_6H_3(NO_2)Me_2$	$C_6H_3(NO_2)_2$·NHMe	$C_6H_3(NO_2)Me_2$
C_6H_5·OH	$C_6H_3(NO_2)_2$·NHMe Polycondensed products	—	*o*-$C_6H_4(NO_2)$·OH
C_6H_5·NMe_2	$C_6H_3(NO_2)_2$·NHMe Condensed products	—	Benzidine derivatives Condensed products

The general conclusions to be drawn from these tests for the production of nitric acid, or other nitrating agent, during the rearrangement of 2 : 4-dinitrophenylmethylnitroamine are that it certainly is produced, and that it can be taken up by an added foreign aromatic compound. Furthermore, by the addition in suitable amount of a sufficiently reactive foreign compound, the original rearrangement can be largely diverted into the interaction which transfers the *N*-nitro-group to the aromatic nucleus of the foreign compound. From this it follows that the speed of production of nitric acid (reaction 2 of the scheme on p. 2678), under the conditions of the rearrangement, cannot be much smaller than that of the rearrangement (total of reactions 1 and 2 + 4), as it would take place in the absence of the foreign compound.

(2.4) *Rearrangement of* 2 : 4-*Dinitrophenylmethylnitramine versus the Nitration of* 2 : 4-*Dinitromethylaniline.*—From the above it follows that, under conditions in which 2 : 4-dinitro-

phenylmethylnitramine is rearranged, nitric acid is produced as rapidly as would allow it to be made responsible for at least a large part of the rearrangement, provided that the nitric acid, when produced, were capable of behaving in the way required. What is required is that nitric acid shall be able, under the same conditions, to convert the other denitration product, 2 : 4-dinitromethylaniline, into the rearrangement product, 2 : 4 : 6-trinitromethylaniline, smoothly and about as rapidly as (or more rapidly than) the rearrangement is observed to take place. The question of whether nitric acid can in fact do this obviously had to be tested.

In one of the media which we have used for the rearrangements, namely, concentrated sulphuric acid, a direct answer to this question was not obtained, for 2 : 4 : 6-trinitromethylaniline was formed in both the rearrangement and the nitration, and the reactions appeared to be fast under our conditions.

For aqueous sulphuric acid media, however, the question at issue could be answered unequivocally. We have already noted that, in 80% (by weight) aqueous sulphuric acid, the rearrangement of 2 : 4-dinitrophenylmethylnitramine is substantially complete after 2 hours at 25°. In parallel with an experiment illustrating this, an experiment was set up in which the 2 : 4-dinitrphenylmethylnitramine was replaced by 2 : 4-dinitromethylaniline, together with one molecular proportion of nitric acid, the medium being the same. After 2 hours at 25° little change had occurred. The two experiments were repeated, with the same medium, in fact with portions of medium taken from the same stock of 80% aqueous sulphuric acid, but with the refinement of adding one molecular proportion extra of water to the 2 : 4-dinitrophenylmethylnitramine, in order to compensate for the extra molecule of water contained in the constitution of the comparison pair of substances, 2 : 4-dinitromethylaniline and nitric acid. The results were as before. This pair of experiments was now repeated allowing various longer periods for reaction, up to 170 hours, at 20°. In all cases the rearrangements of 2 : 4-dinitrophenylmethylnitramine were nearly complete, while in the comparison experiments with 2 : 4-dinitromethylaniline considerable proportions of the unconverted material could be readily recovered, even after the longest of the treatments. Similar results were obtained for the longer reaction periods in some experiments which were carried out with 72% (by weight) aqueous sulphuric acid as the medium.

The principal result of the work reported in this Section may be summarised in the statement that, under those conditions of rearrangement of 2 : 4-dinitrophenylmethylnitramine for which a decision can be made, 2 : 4 : 6-trinitromethylaniline is formed more readily and more smoothly by the rearrangement than it is formed by the interaction of 2 : 4-dinitromethylaniline with nitric acid.

(3) *Discussion of the Mechanism of the Nitramine Rearrangement.*

The experiments described in Section 2 establish the following points: (2.1) that the acid-catalysed rearrangement of phenylnitramine and the nitration of aniline, in comparable conditions, orient the nuclear nitro-substituent in quite different ways; (2.2) that, in the rearrangement of *p*-nitrophenylmethylnitramine, nitric acid is not produced to a detectable extent, and not fast enough to enable it to be considered as a possible intermediate; (2.3) that, in the rearrangement of 2 : 4-dinitrophenylmethylnitramine, nitric acid is produced quickly enough to allow it to be considered as a possible intermediate; (2.4) but that nitric acid cannot actually be an intermediate of any importance, because it does not effect the necessary nuclear nitration with sufficient facility.

From this we conclude that the acid-catalysed rearrangement of nitramines in the solvents investigated—mostly solvents having at least the polarity of acetic acid, and including water and sulphuric acid—is essentially intramolecular. Transference of the nitro-group of the nitramine to a foreign aromatic nucleus can be observed, but this means only that reversible acidolysis of the nitro-group occurs, not that it is responsible for the rearrangement.

We have found no counterpart in the nitramine rearrangement to the reversible acidolysis succeeded by nuclear substitution, which Orton established as the basic mechanism for the rearrangement of aromatic chloramines in polar solvents. However, the nitramine rearrangement is analogous in mechanism to the benzidine change, which Ingold and Kidd proved to be intramolecular (*J.*, 1933, 984). Thus we have the interesting situation that, of the three groups, NHAr, Cl, NO_2, which for many purposes form a monotonic series, and which in aniline derivatives can migrate from nitrogen to the nucleus under the influence of acids, in polar solvents, the first and the third use the internal mechanism, while the second employs the external route. The range of this dichotomy of mechanism in the analogous migrations of other groups is receiving further attention.

(4) Experimental.

(4.1) *Orientation in the Rearrangement of Phenylnitramine and in the Nitration of Aniline.*—Phenylnitramine was prepared by a method essentially the same as that of Bamberger (*Ber.*, **1893**, **26**, 471; **1894**, **27**, 359). Crystallised from light petroleum, it had m. p. 44·5°. Aniline nitrate was prepared from freshly distilled aniline and absolute nitric acid in chloroform solution below −5°. It was crystallised from ethyl alcohol–chloroform. The three nitroanilines needed for the construction of the freezing-point diagram were purified as recommended by Holleman, Hartogs, and Linden (*loc. cit.*). Our *o*-nitroaniline had f. p. 69·2°, the *m*-nitroaniline f. p. 112·1°, and the *p*-nitroaniline f. p. 148·0°, these f. p.s being 0·2—0·3° lower than those recorded by Holleman and his co-workers.

The freezing points were determined by the Beckmann method, with continued observation of the cooling curve in many cases in order to determine the second freezing point.

The preliminary qualitative experiments made in order to ascertain the nature of the main products formed in the rearrangement of phenylnitramine, and in nitration of aniline in comparable conditions, and also to establish the best common condition for a quantitative investigation of the proportions in which the isomeric nitroanilines are formed in these reactions, are sufficiently described in Section 2.1. The quantitative experiments were carried out as follows.

Phenylnitramine (4·0 g.) was added in small portions to well-stirred sulphuric acid monohydrate (120 c.c.) at its freezing point. After being kept overnight, the solution was poured on ice and water (2 l.), and neutralised by means of sodium carbonate. A brown solid separated, and the whole mixture was extracted thoroughly with chloroform. The residue obtained by evaporating the chloroform was distilled twice at 1 mm. in order to remove all traces of tar. The yield was 90%. The initial f. p. was 64·5°, which corresponds to an *o*-nitroaniline content of 93·3%. This product (1·222 g. sample) was mixed with *p*-nitroaniline (1·354 g.). The initial f. p. of the mixture was 111·0°, which corresponds to 55·8% of *p*-nitroaniline, *i.e.*, to 6·8% of it in the original rearrangement product. The rearrangement product (1·153 g.) was mixed with *m*-nitroaniline (1·560 g.). This mixture had the initial f. p. 84·6°, which corresponds to 57·0% of *m*-nitroaniline in the mixture, *i.e.*, to none in the rearrangement product.

Aniline nitrate (4·5 g.) was added to sulphuric acid monohydrate (120 c.c.), and the product was worked up as before. The yield of isolated material was 80%. The initial f. p. was 114·45°, which corresponds to 59·3% of *p*-nitroaniline. This product (0·7809 g.) was mixed with *m*-nitroaniline (1·8290 g.). The mixture had initial f. p. 100·4°, corresponding to 80·2% of *m*-nitroaniline in the mixture, *i.e.*, to 33·8% in the original nitration product. The nitration product (0·3625 g.) was mixed with *o*-nitroaniline (2·4678 g.). This mixture had f. p. 60·7°, which corresponds to 88·0% of *o*-nitroaniline in the mixture, *i.e.*, to 6·3% in the original nitration product.

(4.2) *Rearrangement of* p-*Nitrophenylmethylnitramine.*—*p*-Nitromethylaniline (16 g.), suspended in acetic acid (150 c.c.), was treated with anhydrous nitric acid (7·5 c.c.) and acetic anhydride (30 c.c.). The original yellow solid quickly dissolved and a colourless solid separated. After 1 hour, the mixture was poured into water, and the *p*-nitrophenylmethylnitramine was collected and crystallised from ethyl alcohol. The yield was 16 g., and the m. p. 139° (Found: C, 42·8; H, 3·5. Calc.: C, 42·6; H, 3·5%).

A general account of the experiments, which were made on the rearrangement of this substance by means of various acids, in various solvents, without and with added aromatic compounds, is given in Section 2.2. Details of a few of these experiments are now added as illustration. (*Expt.* 1*a*). The nitramine (0·5 g.) was dissolved in cold concentrated sulphuric acid (10 c.c.), and the yellow solution was at once poured into water. The precipitated solid was collected, crystallised from acetic acid, and identified as 2 : 4-dinitromethylaniline by its m. p., 175·5°, and the mixed m. p. with an authentic specimen. (*Expt.* 2*d*). A solution of the nitramine (0·5 g.) in acetic acid (20 c.c.) was treated with a stream of dry hydrogen chloride, and the brown solution thus obtained was poured into water. The precipitated substance was crystallised from acetic acid, and identified by its m. p., 174·5°, and mixed m. p., as before. (*Expt.* 12*a*). A solution of the nitramine (1 g.) and of *p*-xylene (1 g.) in acetic acid (40 c.c.) was treated with hydrogen chloride. Some crystals separated, which were collected and identified as 2 : 4-dinitromethylaniline. The remaining brown solution was poured into water, and then distilled in steam. The distillate, which contained an oil, was extracted with ether. The ethereal solution was washed with aqueous sodium carbonate and dried. Distillation of the residue obtained by concentration of the extract gave unchanged *p*-xylene. The small residue remaining after the distillation was transferred to an Emich tube and micro-fractionated. In this way a little more *p*-xylene was obtained, the whole of the product distilling well below the b. p. of nitro-*p*-xylene. The material not carried over in the steam-distillation consisted of a yellow solid in aqueous suspension. The solid was collected, crystallised from acetic acid, and identified by its m. p., 174·5°, and mixed m. p., as 2 : 4-dinitromethylaniline.

(4.3) *Rearrangement of* 2 : 4-*Dinitrophenylmethylnitramine.*—The preparation of this substance is described in Part VII. A general account of its behaviour when treated with various acids, with or without solvents, is given in Section 2.3. Details are now added of a few illustrative cases. (*Expt.* 1). The nitramine (0·5 g.) was added to sulphuric acid (5 c.c.) at room temperature. After being kept overnight, the yellow solution was poured into water and the yellow precipitate then formed was collected, crystallised from ethyl alcohol, and identified by its m. p. and mixed m. p. as 2 : 4 : 6-trinitromethylaniline. (*Expt.* 5). The nitramine (0·5 g.) was heated on the water-bath with absolute nitric acid (10 c.c.). The solution became purple and then yellow. After 2·5 hours it was poured on ice, and the precipitate was collected, crystallised from ethyl alcohol, and identified by its m. p. and mixed m. p. as 2 : 4 : 6-trinitrophenylmethylnitramine. (*Expt.* 6). The 2 : 4-dinitro-nitramine (0·5 g.) was heated on the water-bath for 6 hours with a mixture of nitric acid (10 c.c.) and water (10 c.c.). The

formed 2 : 4 : 6-trinitro-nitramine was isolated and identified as before. (*Expt.* 7). The nitramine (0·5 g.) was refluxed with concentrated hydrochloric acid (20 c.c.) for 3 hours. The solid first melted to give an oil, and this subsequently solidified giving an orange-yellow solid, which, after crystallisation from acetic acid, was identified by its m. p. and mixed m. p. as 2 : 4-dinitromethylaniline.

A general account has been given in Section 2.3 of the experiments made on the nitration of "foreign" aromatic compounds by 2 : 4-dinitrophenylmethylnitramine in media in which the latter undergoes rearrangement, and in the nitration of the same aromatic compounds in the same media by the use of nitric acid instead of the nitramine. A record of the substances isolated is contained in Table I. We now add details of a few of these experiments in illustration. (*Expt.* 12). 2 : 4-Dinitrophenylmethylnitramine (4 g.) was added to a mixture of sulphuric acid (40 c.c.) and *p*-xylene (2·5 c.c.). The solution darkened, a yellow oil separating. After being kept overnight, the mixture was poured into water and distilled in steam. The distillate was extracted with ether, and the residue obtained on concentrating the extract was micro-fractionated to give 2-nitro-*p*-xylene, b. p. (Emich) 230—232°, n_D^{20} 1·5468 (Found : C, 63·2, 63·6; H, 6·6, 6·2; N, 9·2. Calc. : C, 63·5; H, 6·0; N, 9·3%). The solid product not carried over by the steam was collected, crystallised twice from acetic acid, and identified as 2 : 4-dinitromethylaniline by its m. p. and mixed m. p. There were indications of the formation also of 2 : 4 : 6-trinitromethylaniline,but this substance was not isolated in a pure state. (*Expt.* 12*a*). Nitric acid (0·5 g.) was added to a mixture of sulphuric acid (25 c.c.) and *p*-xylene (1·2 c.c.). The product was worked up as in the preceding experiment. The steam-volatile material was solid, and from it, by crystallisation from ethyl alcohol, colourless needles, m. p. 93°, were obtained, corresponding in properties to 2 : 3-dinitro-*p*-xylene. (*Expt.* 24). 2 : 4-Dinitrophenylmethylnitramine (2g.) was added to a mixture of dimethylaniline (1 g.) and 80% (by weight) aqueous sulphuric acid (28·5 c.c.). Oxides of nitrogen were produced. After being left overnight, the mixture was poured into water, and the formed precipitate was collected, and crystallised repeatedly from ethyl alcohol. 2 : 4-Dinitromethylaniline, identified by m. p. and mixed m. p., was obtained. The aqueous filtrate was made alkaline, and some unchanged dimethylaniline was removed by distillation in steam. A tarry residue was left, which was dissolved in aqueous hydrochloric acid and cleaned as much as possible with charcoal. On basification with sodium carbonate, a pale pink solid was recovered with the properties of somewhat impure tetramethylbenzidine. There was evidence of the presence of a red compound, which may have been the 3 : 3′-dinitro-derivative (see below), but this was not isolated. (*Expt.* 24*a*). Nitric acid (0·5 g.) was added to a mixture of dimethylaniline (1 g.) and 80% aqueous sulphuric acid (28·5 c.c.). The solution became yellow, and then red. After being left overnight, it was poured into water. No precipitate appeared, but, when the solution was basified with sodium carbonate, a red solid separated. This was collected and extracted with hot ethyl alcohol. On concentration of the extract, and crystallisation of the solid obtained repeatedly from ethyl alcohol and from benzene–light petroleum, red crystals were obtained, m. p. 186°, probably 3 : 3′-dinitrotetramethylbenzidine. Indications were obtained of the presence also of unsubstituted tetramethylbenzidine, but this compound was not isolated pure.

An account of the series of experiments, which were made in order to compare the ease of rearrangement of 2 : 4-dinitrophenylmethylnitramine with the facility and the course of nitration of 2 : 4-dinitromethylaniline by nitric acid in comparable conditions, has been given in Section 2.4. Details of a few experiments are supplied as illustration. (*Expt.* 1). The nitramine (1·84 g.) was added to sulphuric acid (50 g.) at room temperature. After 24 hours the solution was poured into water (250 c.c.), the precipitate was collected (m. p. 109°, yield 93%), and, after crystallisation from alcohol, the product was identified as 2 : 4 : 6-trinitromethylaniline by comparison with an authentic specimen. (*Expt.* 1*a*). 2 : 4-Dinitromethylaniline (1·50 g.) and nitric acid (0·52 g.) were added to sulphuric acid (50 g.), and the solution was treated as before. The product (m. p. before purification 111°, yield 94%) was crystallised once from alcohol, and identified by its m. p. 113°, and mixed m. p., as 2 : 4 : 6-trinitromethylaniline. (*Expt.* 11). The nitramine (1·84 g.) and water (0·14 g.) were added to a portion (50 g.) of medium drawn from a made-up stock of 80% aqueous sulphuric acid. After 170 hours at 20°, the solution was poured into water, and the total product was recovered. It had m. p. 102°, and was somewhat impure 2 : 4 : 6-trinitromethylaniline, which could be obtained pure by crystallisation from alcohol. (*Expt.* 11*a*). 2 : 4-Dinitromethylaniline (1·50 g.) and nitric acid (0·52 g.) were added to a portion (50 g.) of the same stock of 80% sulphuric acid. After 170 hours at 20°, the total product was recovered as before. It had m. p. 130° and consisted of impure 2 : 4-dinitromethylaniline, which was readily obtained pure by washing it with benzene and crystallising it from acetic acid.

UNIVERSITY COLLEGE OF NORTH WALES, BANGOR.
WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1.

[*Received, December 17th,* 1949.]

515. *Synthesis and Configuration of (+)-6-Methyloctanoic Acid, a Degradation Product of the Polymyxins.*

By Leslie Crombie and Stanley H. Harper.

Hydrolytic degradation of the polymyxins, a series of related antibiotics from *B. polymyxa*, gives a dextrorotatory nitrogen-free acid, $C_9H_{18}O_2$, together with amino-acids. By oxidative degradation earlier workers have identified this acid as 6-methyloctanoic acid.

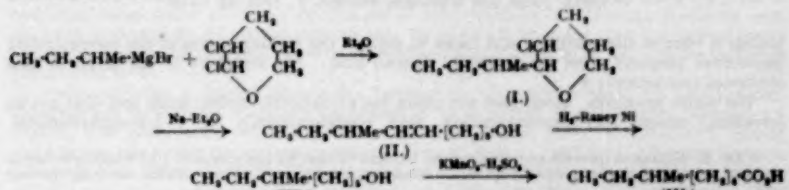
By the method, devised by us, of chain extension by four methylene groups at a time, (−)-2-methylbutanol is converted in four stages into (+)-6-methyloctanol, which on oxidation yields (+)-6-methyloctanoic acid, identical with the naturally derived acid. This synthesis relates 6-methyloctanoic acid configurationally, through 2-methylbutanol, to glyceraldehyde. The deduction that the (+)-acid has the L-configuration is criticised and a new configurational series based on 2-methylbutanol is proposed.

A similar synthesis, utilising the method of chain extension by five methylene groups at a time, yields (±)-6-methyloctanoic acid in four stages from (±)-*sec.*-butyl bromide.

The culture media of strains of *B. polymyxa* contain a series of related antibiotics which are now designated as polymyxins A, B, C, D, and E (Brownlee and Jones, *Biochem. J.*, 1948, **43**, xxv; various authors, Proc. of a Conference on Antibiotics derived from *B. polymyxa*, *Ann. New York Acad. Sci.*, 1949, **51**, 855 *et seq.*). They are considered to be cyclic peptides and on degradation all give threonine, αγ-diaminobutyric acid, and a dextrorotatory nitrogen-free acid, $C_9H_{18}O_2$, together with one or more of leucine, phenylalanine, and serine (Jones, *Biochem. J.*, 1948, **43**, xxvi; Catch, Wilkinson, and Jones, *ibid.*, p. xxvii). Comparison of the infra-red absorption spectrum of the C_9 acid with that of pelargonic (*n*-nonanoic) acid suggested a branched-chain structure for the former (Gore and Petersen, *Ann. New York Acad. Sci.*, 1949, **51**, 924), and Wilkinson (*Nature*, 1949, **164**, 622) has recently degraded this acid to (+)-3-methylpentanoic acid by the Miescher extension of the Barbier–Wieland degradation (*Helv. Chim. Acta*, 1944, **27**, 1815; 1945, **28**, 1252). The C_9 acid from the polymyxins is thus (+)-6-methyloctanoic acid, an acid which has previously been stated to occur in degras (wool fat) (Weitkamp, *J. Amer. Chem. Soc.*, 1945, **67**, 447). This communication is concerned with the synthesis of (±)- and (+)-6-methyloctanoic acid and the deduction of the configuration of the latter relative to glyceraldehyde.

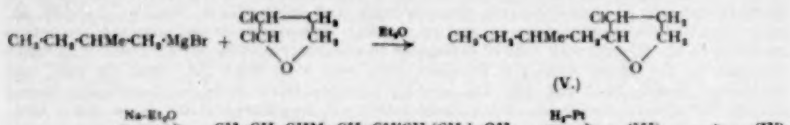
Levene and Marker (*J. Biol. Chem.*, 1932, **95**, 153; 1933, **103**, 299) prepared an active 6-methyloctanoic acid from *sec.*-butyl bromide by an eleven-stage synthesis and resolution. This lengthy route was clearly not intended as a preparative method, interest being centred on the optical rotations of the intermediates. A preparative method for the (±)-acid was described by Cason and Prout (*J. Amer. Chem. Soc.*, 1944, **66**, 46) who used a five-stage synthesis starting from adipic acid, in which ethyl 6-ketoheptanoate was prepared by the action of dimethylcadmium on 3-carbethoxyvaleryl chloride. Reaction of ethyl 6-ketoheptanoate with ethylmagnesium iodide, dehydration of the resulting hydroxy-ester, and catalytic hydrogenation yielded ethyl 6-methyloctanoate. The dehydration, by distillation with iodine, caused difficulty and the overall yield from ethyl 6-ketoheptanoate was only 20%, other reagents being even less satisfactory. Another method (Cason and Prout, *loc cit.*), based on the reaction of β-carbomethoxypropionyl chloride with di-2-methylbutylcadmium and subsequent Clemmensen reduction, yielded only an impure product, although this was attributed to the presence of *iso*amyl alcohol in the starting material.

The methods of chain extension by four and five methylene groups devised by us recently (Crombie and Harper, *J.*, 1950, 1707, 1714), based on the ring scission of 2-alkyl-3-chlorotetrahydro-furans and -pyrans respectively, appeared to offer more attractive routes to the racemic, and particularly to an optically active, acid whose configuration could be related to that of known substances. For (±)-6-methyloctanoic acid we have employed the second of these methods, as follows:



The mixed *cis*- and *trans*-2-*sec.*-butyl-3-chlorotetrahydropyrans (I), from the interaction of *sec.*-butylmagnesium bromide and 2 : 3-dichlorotetrahydropyran, were not separated but were subjected to ring scission to give, what is almost certainly in the light of our earlier experience, pure (±)-*trans*-6-methyloct-4-en-1-ol (II). Both this alcohol and the (±)-6-methyloctanol (III) obtained on reduction were characterised by crystalline 4-diphenylylurethanes. Unexpectedly, oxidation of (±)-6-methyloctanol with alkaline potassium permanganate failed (cf. Fournier, *Bull. Soc. chim.*, 1909, [iv], **5**, 920). However, oxidation in acid solution readily gave (±)-6-methyloctanoic acid (IV), which was characterised as the amide, the *p*-bromophenacyl ester, and the *S*-benzylthiuronium salt (see Table). Incidentally, this method provides a much improved route to (±)-6-methyloctanol which was used by Cason and Prout (*loc. cit.*) as an intermediate for the synthesis of (±)-16-methyloctadecanoic acid.

For the synthesis of an optically active 6-methyloctanoic acid we selected the first of the above methods of chain extension, for this permitted starting from the more accessible optically pure (−)-2-methylbutanol (" active " amyl alcohol from fusel oil) rather than an active *sec.*-butyl alcohol. Furthermore formation and reaction of the primary Grignard reagent should be possible with little, if any, racemisation. It is relevant that Whitmore and Olewine (*J. Amer. Chem. Soc.*, 1938, **60**, 2570) were able to convert (−)-2-methylbutanol into (+)-2-methylbutyl bromide, and thence through the Grignard reagent back into the alcohol with less than 10% racemisation. The method is as follows :



Again the mixed *cis*- and *trans*-3-chloro-2-2′-methylbutyltetrahydrofurans (V), from the interaction of (+)-2-methylbutylmagnesium bromide and 2 : 3-dichlorotetrahydrofuran, were subjected directly to ring scission to give 6-methyloct-3-en-1-ol (VI), which in the light of our previous experience may be a *cis*–*trans*-mixture in which the latter predominates. When this optically active 6-methyloct-3-en-1-ol was hydrogenated overnight in ether in presence of palladium on barium sulphate, a substantial amount of (+)-3-methyloctane was obtained. Hydrocarbon formation under these conditions, either by dehydration and subsequent further reduction or by direct hydrogenolysis, is unusual. Brief hydrogenation in presence of pre-reduced platinum oxide catalyst without a solvent gave (+)-6-methyloctanol in high yield. Again oxidation with alkaline potassium permanganate failed, but (+)-6-methyloctanol was smoothly oxidised in acid solution to (+)-6-methyloctanoic acid. The optical rotation of this acid (see Table) was identical, within the limit of experimental error, with that recorded for the naturally derived acid from the polymyxins. Through the kindness of Dr. W. G. Malcolm of the Lederle Laboratories Division of the American Cyanamid Company we have been able to make a direct comparison of these two acids. The *S*-benzylthiuronium salt and the *p*-bromophenacyl ester of the synthetic acid failed to depress the melting points of the corresponding derivatives prepared from the naturally derived acid. The structure of the latter is thus confirmed synthetically.†

6-Methyloctanoic acid.	B. p./mm.	n_D^{20}.	$[\alpha]_{5461}$ in Et_2O.	Amide, m. p.	*p*-Bromophenacyl ester, m. p.	*S*-Benzylthiuronium salt, m. p.
Synthetic (±)- ...	148—150°/23	1·4337	—	91°	57—58°	150·5°
Synthetic (+)- ...	148—149°/21	1·4330	+8·9°	90—91	58—59	149·5
Natural (+)-	—	1·4325	+8·6 •	93 •	57·0—57·5	148—149

• Catch, Jones, and Wilkinson, *Biochem. J.*, 1948, **43**, xxvii.

The above synthesis, which does not affect the asymmetric carbon atom and thus avoids inversion, relates (+)-6-methyloctanoic acid configurationally to (−)-2-methylbutanol.

† Dr. S. Wilkinson (private communication) informs us that he has prepared (±)-6-methyloctanoic acid and resolved it to give the (+)-acid, which likewise proved to be identical with the naturally derived acid.

Furthermore the specific rotation of the product indicates that little, if any, racemisation occurred. (−)-2-Methylbutanol (" active " amyl alcohol) has long been described as the *d*-form and this is still persisted in. The prefix *d*- merely indicates that on oxidation the alcohol gives dextrorotatory valeric acid [(+)-2-methylbutanoic acid] (Marckwald, *Ber.*, 1902, **35**, 1595; Whitmore, " Organic Chemistry," Chapman and Hall, London, 1937, p. 125) and it is desirable to discontinue the use of this prefix since it is being confused with the real configuration [*e.g.*, *Chem. Abs.*, 1948, **42**, 9840, lists an entry referring to (−)-2-methylbutanol from fusel oil under D-(−)]. On the contrary the following argument can be developed relating (−)-2-methylbutanol, and hence (+)-6-methyloctanoic acid, to L-(−)-glyceraldehyde. First, (−)-2-methylbutanol has the same configuration as (−)-methylsuccinic acid. This follows from the argument of Freudenberg (" Stereochemie," F. Deuticke, Leipzig, 1933, p. 680), which has since been confirmed by interconversions through 3-methyladipic acid. Brown, Kharasch, and Chao (*J. Amer. Chem. Soc.*, 1940, **62**, 3435) converted (−)-2-methylbutanol through (+)-1-chloro-2-methylbutane into (−)-1 : 4-dichloro-2-methylbutane, the enantiomorph of which had earlier been obtained by von Braun and Jostes (*Ber.*, 1926, **59**, 1091) from the degradation of (+)-3-methyladipic acid. von Braun and Jostes later (*ibid.*, p. 1444) degraded (+)-3-methyladipic acid in the same manner to (+)-1 : 4-dibromo-2-methylbutane and converted this into (+)-2-methylbutane-1 : 4-diol and by further oxidative degradation into (+)-methylsuccinic acid. This configurational relationship is further supported by Ställberg-Stenhagen (*Arkiv Kemi Min., Geol.*, 1946, **23**, *A*, No. 15) who converted (+)-2-methylpent-4-enoic acid into (+)-2-methylpentanoic acid by hydrogenation, into (+)-2-methyldecanoic and (+)-2-methylhexacosanoic acids by chain extension from the vinyl group, and subsequently (Ställberg-Stenhagen and Stenhagen, *ibid.*, 1947, **24**, *B*, No. 9) by direct oxidation into (−)-methylsuccinic acid. By analogy these authors assigned (+)-2-methylbutanoic acid and hence (−)-2-methylbutanol the same configuration as (−)-methylsuccinic acid. Secondly, (−)-methylsuccinic acid has the same configuration as (−)-malic acid. This follows from the work of Fredga, who made use of the method of " quasi-racemic compound " formation (cf. " The Svedberg Commemorative Volume," Uppsala, 1944, p. 261). (−)-Methylsuccinic acid was related to (−)-mercaptosuccinic acid through the formation of a quasi-racemic compound between the former and (+)-mercaptosuccinic acid (Fredga, *Arkiv Kemi Min., Geol.*, 1942, **15**, *B*, No. 23), while (−)-" ethylxanthogenosuccinic acid " was related to (+)-" dithiocarbethoxyoxysuccinic acid " through formation of a quasi-racemic compound between the latter and (+)-" ethylxanthogenosuccinic acid " (Fredga, *ibid.*, 1941, **14**, *B*, No. 27). Holmberg (*ibid.*, 1916, **6**, No. 1) had converted (−)-" ethylxanthogenosuccinic acid " into (−)-mercaptosuccinic acid and subsequently (*Ber.*, 1925, **58**, 1822) prepared (+)-" dithiocarbethoxyoxysuccinic acid " from (−)-malic acid. In neither chemical transformation is the bond to the asymmetric carbon atom broken, hence (−)-malic acid is related to (−)-mercaptosuccinic acid and thence to (−)-methylsuccinic acid. Thirdly, (−)-malic acid has the same configuration as L-(−)-glyceraldehyde. This follows from the argument of Freudenberg and Lux (*ibid.*, 1928, **61**, 1083) relating (−)-malic acid to (+)-lactic acid, which Freudenberg (*ibid.*, 1914, **47**, 2027) had earlier converted into (+)-glyceric acid; and (−)-glyceric acid had been obtained by oxidation of D-(+)-glyceraldehyde (Wohl and Schellenberg, *ibid.*, 1922, **55**, 1404). Further support for the configurational relationship of (+)-lactic acid to L-(−)-glyceraldehyde has recently been provided by Wolfrom, Lemieux, Olin, and Weisblat (*J. Amer. Chem. Soc.*, 1949, **71**, 4057). This relationship, however, involves the convention that the carboxyl group of the lactic acid arises from the aldehyde group of glyceraldehyde and not from the primary alcohol group (cf. Freudenberg, " Sterochemie," p. 679; Wolfrom, Lemieux, and Olin, *J. Amer. Chem. Soc.*, 1949, **71**, 2870). Similar conventions arise in the inter-relationship of 2-methylbutanol and methylsuccinic acid, where the primary alcohol group is converted into carboxyl, and with 3-methyladipic acid. Furthermore the correlation of methylsuccinic acid with malic acid, in which a methyl group takes the place of hydroxyl, raises doubt as to the significance of configurational relationships involving such contrasting change at the asymmetric centre; for it should be noted that the methyl group of 2-methylbutanol corresponds, not with the methyl group of lactic acid, but with the hydroxyl group of the latter.

Hence although a formal relationship between (−)-2-methylbutanol and L-(−)-glyceraldehyde can be deduced it appears so tenuous as to be devoid of significance. Instead, we suggest that compounds containing the asymmetric carbon atom, ·C′·CHMe·C″·, should constitute a new configurational series, designated by D_a- and L_a-, with D_a-(+)-2-methylbutanol (subscript " a " indicating " active " amyl alcohol; similar designations for the glyceraldehyde and the amino-acid series have been suggested, see *Chem. Eng. News*, 1947, **25**, 1364) as the

standard of reference, written on the Fischer convention as (VII). For determining unambiguously configurational relationships within this series for the compounds discussed above, three conventions appear necessary. First, that the hydrogen and methyl attached to the asymmetric atom remain unchanged. Second, that in monocarboxylic acids (or other monofunctional compounds) the carboxyl group be derived by oxidation of, or by chain extension from, the primary alcohol group. Third, that in dicarboxylic acids (or other difunctional compounds) the carboxyl group nearer to the asymmetric atom be derived from the primary alcohol group.* On this scheme (−)-2-methylbutanol and hence (+)-6-methyloctanoic acid have the L$_+$-configuration.

(VII.)

Experimental.

Microanalyses and determinations of optical rotation are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorr.

(±)-2-*sec.*-*Butyl*-3-*chlorotetrahydropyran*.—By the procedure used for the preparation of 3-chloro-2-methyltetrahydropyran (Crombie and Harper, *J.*, 1950, 1707), dihydropyran (84 g., 1·0 mol.) was chlorinated at 0—5° in dry ether (200 ml.), and the resulting solution of 2 : 3-dichlorotetrahydropyran added slowly to the well-stirred Grignard reagent prepared from *sec.*-butyl bromide (205 g., 1·5 mols.) and magnesium (36 g.) in dry ether (250 ml.). When one-fifth of the dichlorotetrahydropyran remained to be added solid separated and stirring became impossible, so that the remainder was added with vigorous shaking. Next day the product was isolated as described previously. Distillation of the product gave a considerable lower-boiling fraction (17·5 g.), b. p. <60°/15 mm., n_D^{25} 1·4389, followed by the crude mixed *cis*–*trans*-(±)-2-*sec.*-*butyl*-3-*chlorotetrahydropyrans* (81 g.), b. p. 60—94°/15 mm. On redistillation a portion of the main fraction had b. p. 86—88°/17 mm., n_D^{25} 1·4594 (Found : Cl, 20·6. $C_9H_{17}OCl$ requires Cl, 20·1%). On the assumption that the lower-boiling fraction eliminated at the next stage was present in this crude product, the yield was only 37% (on the dihydropyran), noticeably lower than with the isomeric primary bromide (Crombie and Harper, *loc. cit.*).

(±)-*trans*-6-*Methyloct*-4-*en*-1-*ol*.—By the procedure used for the ring scission of 3-chloro-2-methyltetrahydropyran (Crombie and Harper, *loc. cit.*) the crude mixed *cis*–*trans*-(±)-2-*sec.*-butyl-3-chlorotetrahydropyrans (76 g.) were added dropwise to a stirred suspension of powdered sodium (22 g.) in dry ether (200 ml.). Next day the product was isolated and distilled, to give a fraction (15 g.), b. p. 52—80°/10 mm., n_D^{25} 1·4363 (which from its odour and refractive index was probably the lower-boiling impurity not eliminated at the previous stage), followed by an intermediate fraction (6·5 g.), b. p. 80—94°/10 mm., n_D^{25} 1·4416, and then pure (±)-*trans*-6-*methyloct*-4-*en*-1-*ol* (42 g., 85% on pure alkylchlorotetrahydropyran), b. p. 94—95°/10 mm., n_D^{25} 1·4463 (Found : C, 75·4; H, 12·65. $C_9H_{18}O$ requires C, 76·0; H, 12·75%). The 4-*diphenylylurethane* crystallised from light petroleum (b. p. 80—100°) in prisms, m. p. 85·5° (Found : C, 78·55; H, 8·0; N, 4·2. $C_{22}H_{27}O_2N$ requires C, 78·3; H, 8·05; N, 4·15%).

(±)-6-*Methyloctan*-1-*ol*.—(±)-*trans*-6-Methyloct-4-en-1-ol (22·7 g.) was hydrogenated without a solvent in the presence of Raney nickel (*ca.* 1 g., damp with ethanol) until absorption of hydrogen ceased (uptake : 3·64 l. at N.T.P. Calc. for 1 mol. 3·57 l.). Filter cel was added and the catalyst filtered off and rinsed with ether. Distillation of the filtrate gave (±)-6-methyloctan-1-ol (22·3 g., 95%), b. p. 112—114°/23 mm., n_D^{25} 1·4350 (Found : C, 74·0; H, 13·35. Calc. for $C_9H_{20}O$: C, 74·9; H, 13·95%). The 4-*diphenylylurethane* formed crystals, m. p. 99·5°, of ill-defined shape from light petroleum (b. p. 80—100°) (Found : C, 77·7; H, 8·45; N, 4·3. $C_{22}H_{29}O_2N$ requires C, 77·8; H, 8·6; N, 4·15%).

(±)-6-*Methyloctanoic Acid*.—(±)-6-Methyloctanol (6·0 g.) was dispersed in a cold solution of sulphuric acid (12·0 g.) in water (80 ml.) by vigorous stirring, and powdered potassium permanganate (9·0 g.) was added as fast as it was reduced, whilst the temperature was kept below 25°. Sufficient solid sodium hydrogen sulphite was then added to dissolve the manganese dioxide, and the solution thoroughly extracted with ether. The ethereal extracts were extracted with 20% sodium hydroxide. This alkaline extract was covered with light petroleum (b. p. 40—60°), and the acid liberated by acidification (Congo-red) with 30% sulphuric acid. Evaporation and distillation gave pure (±)-6-methyloctanoic acid (4·30 g., 66%), b. p. 148—150°/23 mm., n_D^{25} 1·4337 (Found : C, 68·4; H, 11·25. Calc. for $C_9H_{18}O_2$: C, 68·3; H, 11·45%). The amide, prepared by treatment of the acid chloride with aqueous ammonia (*d* 0·880), crystallised as plates, m. p. 91°, from ether–light petroleum (b. p. 40—60°). This acid was further characterised as the *p*-*bromophenacyl* ester, plates (from aqueous ethanol), m. p. 57—58° (Found : C, 57·65; H, 6·55. $C_{17}H_{23}O_3Br$ requires C, 57·45; H, 6·5%), and as the *S*-*benzylthiuronium* salt, plates (from aqueous ethanol), m. p. 150·5° (Found : C, 63·3; H, 8·55. $C_{17}H_{28}O_2N_2S$ requires C, 62·95; H, 8·7%).

(+)-2-*Methylbutyl Bromide*.—(−)-2-Methylbutanol, isolated from fusel oil by fractional distillation through a many-plate column, had $[\alpha]_D^{18}$ −9·44° (*l*, 2), which on the assumption of d_4^{18} = 0·818 gives $[\alpha]_D^{18}$ −5·77°. Marckwald and McKenzie (*Ber.*, 1901, **34**, 485) recorded $[\alpha]_D^{20}$ −5·90° for pure (−)-2-methylbutanol isolated by fractional crystallisation of the 3-nitrophthalate, Marckwald (*ibid.*, 1902, **35**, 1595) recorded $[\alpha]_D$ −5·82° for pure alcohol obtained by fractional crystallisation of the barium alkyl sulphate, and Whitmore and Olewine (*J. Amer. Chem. Soc.*, 1938, **60**, 2569) have recorded $[\alpha]_D^{25}$ −6·04° for alcohol isolated by fractional distillation (100-plate column). We therefore regard this material as substantially optically pure (<98%) and are particularly indebted to Drs. M. P. Balfe and J. Kenyon for procuring it for us.

* We are indebted to the Editor for the interest he has shown and the help he has given in the elucidation of this stereochemical problem.

Phosphorus tribromide (18·5 g.) was added slowly to a mixture of the above (−)-2-methylbutanol (15·0 g.) and pyridine (4·65 g.) kept at 0°. After a further 2 hours the crude bromide (24·2 g.) was isolated by distillation at 300 mm., heating being discontinued when the orange residue in the flask seethed. The distillate was diluted with light petroleum (b. p. 40—60°) and washed successively with 5% sodium hydroxide, 10% sulphuric acid, concentrated sulphuric acid, and water. After drying ($CaCl_2$), distillation gave (+)-2-methylbutyl bromide (17·0 g., 66%), b. p. 118—120°, n_D^{20} 1·4352, $[\alpha]_D^{20}$ +5·81° (*c*, 4·8 in chloroform) (Found: C, 39·75; H, 7·35; Br, 52·9. Calc. for $C_5H_{11}Br$: C, 40·05; H, 7·35; Br, 53·3%). Whitmore and Olewine (*ibid.*, p. 2570) isolated only a 29% yield, by a similar procedure, of bromide, n_D^{20} 1·4450.

"*Active*" 3-*Chloro*-2-2′-*methylbutyltetrahydrofuran*.—By the procedure used for 3-chloro-2-methyltetrahydrofuran (Crombie and Harper, *J.*, 1950, 1714) freshly distilled 2 : 3-dichlorotetrahydrofuran (5·5 g., 1·0 ml.) was diluted with ether (5 ml.) and added slowly with stirring to the Grignard reagent prepared from magnesium (1·08 g.) and (+)-2-methylbutyl bromide (6·8 g., 1·15 mols.) in dry ether (25 ml.). After brief refluxing the product was isolated as described previously. Distillation eliminated a forerun (1·5 g.), b. p. 40—74°/21 mm., n_D^{20} 1·4280, and then gave mixed "active" cis–trans-3-*chloro*-2-2′-*methylbutyltetrahydrofuran* (3·56 g., 52%), b. p. 104—110°/21 mm., n_D^{20} 1·4580, which was used for the next stage without further purification. In another experiment, however, on redistillation the product had b. p. 85—90°/11 mm., n_D^{20} 1·4600 (Found: Cl, 19·6. $C_9H_{17}OCl$ requires Cl, 20·05%).

"*Active*" 6-*Methyloct*-3-*en*-1-*ol*.—By the procedure used for the ring scission of 2-*sec.*-butyl-3-chlorotetrahydropyran, the mixed "active" *cis–trans*-3-chloro-2-2′-methylbutyltetrahydrofuran (3·56 g.) was added to powdered sodium (1·05 g.) suspended in dry ether (10 ml.). Isolation of the product as already described gave "active" cis–trans-6-*methyloct*-3-*en*-1-*ol* (2·22 g., 78%), b. p. 91—92°/10 mm., 109—110°/22 mm., n_D^{20} 1·4493 (Found: C, 75·8; H, 12·75. $C_9H_{18}O$ requires C, 76·0; H, 12·75%).

(+)-6-*Methyloctan*-1-*ol*.—The above 6-methyloct-3-en-1-ol (2·12 g.) was hydrogenated without a solvent over a platinum oxide catalyst (100 mg.) (uptake: 326 ml. at N.T.P. Calc. for 1 mol. 334 ml.). Isolation as described for the (±)-isomer gave (+)-6-*methyloctanol* (1·90 g., 89%), b. p. 111—113°/22 mm., n_D^{20} 1·4350, $[\alpha]_D^{20}$ +7·21° (*c*, 6·4 in chloroform) (Found: C, 75·0; H, 13·9. $C_9H_{20}O$ requires C, 74·9; H, 13·95%). The 4-*diphenylylurethane* had m. p. 100° (Found: C, 77·95; H, 8·5; N, 4·05. $C_{22}H_{29}O_2N$ requires C, 77·8; H, 8·6; N, 4·15%).

In another reduction of 6-methyloct-3-en-1-ol (2·59 g.) with palladium on barium sulphate (150 mg.: 5% Pd) in ether, hydrogenation was continued overnight until there was no further uptake (not measured). The product was heterogeneous and on distillation gave the fractions: (i) b. p. 32—42°/10 mm., n_D^{20} 1·4080 (610 mg.); (ii) b. p. 42—96°/10 mm., n_D^{20} 1·4350 (530 mg.); and (iii) b. p. 96°/10 mm., n_D^{20} 1·4355 (910 mg.). Redistillation of (ii) and (iii) gave pure (+)-6-methyloctanol, b. p. 97°/11 mm., n_D^{20} 1·4358. Redistillation of (i) gave (+)-3-methyloctane, b. p. 144°/760 mm. (Emich method), n_D^{20} 1·4081, $[\alpha]_{5461}^{20}$ +8·39°, $[\alpha]_{5780}^{20}$ +7·54° (*c*, 9·8 in chloroform) (Found: C, 83·95; H, 15·4. Calc. for C_9H_{20}: C, 84·3; H, 15·7%).

(+)-6-*Methyloctanoic Acid*.—(+)-6-Methyloctanol (1·0 g.) was oxidised with potassium permanganate (1·5 g.) in 20% sulphuric acid (15 ml.) as described for the (±)-isomer. Distillation of the product gave (+)-6-methyloctanoic acid (660 mg., 60%), b. p. 148—149°/21 mm., n_D^{20} 1·4330, $[\alpha]_{5461}^{20}$ +8·9°, $[\alpha]_{5780}^{20}$ +7·9° (*c*, 10·2 in ether). This acid was characterised as the amide, m. p. 90—91°, as the *p-bromophenacyl* ester, plates (from aqueous ethanol), m. p. 58—59° (Found: C, 57·8; H, 6·6. $C_{17}H_{23}O_3Br$ requires C, 57·45; H, 6·5%), and as the S-*benzylthiuronium* salt, glistening plates (from aqueous ethanol), m. p. 149·5° (Found: C, 63·0; H, 8·7. $C_{17}H_{28}O_2N_2S$ requires C, 62·95; H, 8·7%).

C$_9$ *Acid Derived from the Polymysins*.—The sample of slightly impure naturally derived acid (0·2 ml.) was pale brown and had an odour somewhat different odour to that of the synthetic acid. It was characterised as the *p*-bromophenacyl ester, plates (from aqueous ethanol), m. p. 57·0—57·5° [mixed m. p. with the corresponding derivative of the synthetic (+)-acid, 57—58°], and as the *S*-benzylthiuronium salt, glistening plates (from aqueous ethanol), m. p. 148—149° [mixed m. p. with the corresponding derivative of the synthetic (+)-acid, 149·5°].

KING'S COLLEGE (UNIVERSITY OF LONDON), STRAND, W.C.2. [*Received, June 12th*, 1950.]

---

516. *Organic Fluorides. Part III. Fluorination of Aromatic Hydrocarbons by Use of a Gold Catalyst.*

By R. N. HASZELDINE and F. SMITH.

The action of fluorine upon aromatic hydrocarbons in the vapour phase in the presence of a gold catalyst and an inert gas affords fluorocarbons. The latter contain only carbon and fluorine and are believed to possess the same carbon skeleton as the parent hydrocarbon.

IN Part I (Musgrave and Smith, *J.*, 1949, 3021) it was demonstrated that fluorination of hydrocarbons in the presence of a silver catalyst is greatly facilitated by carrying out the reaction at elevated temperatures (200—300°), and in Part II (*idem*, *ibid.*, p. 3026) the evidence indicated that, among several metals examined, gold was the most effective catalyst for the vapour-phase fluorination of benzene. This communication and Part IV (*J.*, 1950, paper no. 536) deal

with the application of these findings to the fluorination of a number of aromatic and alicyclic hydrocarbons. By controlling the conditions fluorocarbons can be produced in yields not previously attainable by other direct fluorination techniques which employed lower temperatures (Bockemüller, *Annalen*, 1933, **506**, 20; Fredenhagen and Cadenbach, *Ber.*, 1934, **67**, 928; Bigelow *et al.*, *J. Amer. Chem. Soc.*, 1933, **55**, 4614; see also Bigelow, *Chem. Rev.*, 1947, **40**, 51).

This investigation was made in order to determine the effects of temperature, rate of addition of fluorine and hydrocarbon, and dilution of fluorine and of hydrocarbon with nitrogen upon the yield of fluorocarbon, and to obtain sufficient pure material to enable the physical properties of the fluorocarbons to be studied.

The general effects of the variables were as follows: An increase in the nitrogen dilution favoured the production of hydrofluorocarbon, and a decrease in nitrogen dilution increased the decomposition. When the reaction temperature was increased the yield of the required fluorocarbon rose to a maximum and then fell as decomposition proceeded more rapidly. Increasing the amount of fluorine caused extensive degradation and a consequent reduction in the yield of the required fluorocarbon. Decreasing the rate of hydrocarbon addition resulted occasionally in an increase in the yield of fluorocarbon with little increase in the amount of decomposition, and an increase in the rate of addition sometimes gave an increase in hydrofluorocarbon with little alteration in the yield of fluorocarbon. The latter effect was of value since the hydrofluorocarbon could be recycled.

Most hydrocarbons upon fluorination give rise to varying amounts of polymeric products, some of which appear to have possibilities as lubricants and insulators. This polymer formation is controllable to a certain degree by the choice of starting material and by the reaction conditions. Unsaturated hydrocarbons appeared to polymerise to a somewhat greater extent than the corresponding saturated hydrocarbon (cf. McElvain and Langston, *J. Amer. Chem. Soc.*, 1944, **66**, 1749; see Part IV) and it was also observed that high addition rates and high nitrogen dilution favoured polymerisation.

It was shown that perfluoro*cyclo*hexane is readily obtained from benzene at 280° (cf. Part I). At lower temperatures the yield of perfluoro*cyclo*hexane was greatly reduced. This was expected from the pioneering experiments of Bigelow and Fukuhara, who obtained small amounts of perfluoro*cyclo*hexane by the action of fluorine diluted with nitrogen upon benzene at 90° in the presence of copper gauze (*J. Amer. Chem. Soc.*, 1941, **63**, 2792).

Perfluoromethyl*cyclo*hexane was produced by fluorination of toluene at 250°. It was obtained in still higher yields from benzotrifluoride, a result probably due to the fact that benzotrifluoride is more stable than toluene under the conditions of fluorination. Similar results have already been reported by Cady and his co-workers (*Ind. Eng. Chem.*, 1947, **39**, 290).

Fluorocarbons of the formula C_9F_{18} were obtained by fluorination of technical xylene, *o*-xylene, *m*-xylene, bistrifluoromethylbenzene, and ethylbenzene. Although good yields were produced from technical xylene, the most readily available hydrocarbon which would give rise to C_9F_{18}, better yields resulted from the *m*- than from the *o*-isomer and still higher yields were produced from ethylbenzene.

Contrary to expectation, the fluorination of 1 : 3-bistrifluoromethylbenzene appeared to indicate that this was not a good starting material for the preparation of C_9F_{18} since extensive polymerisation occurred.

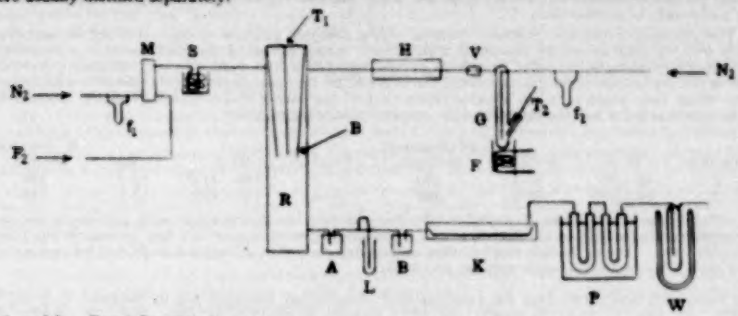
Mesitylene proved to be a convenient substance for the production of C_9F_{18} but it suffered more decomposition than either xylene or toluene. *p*-Cumene, less symmetrical and presumably less stable than mesitylene during fluorination, gave a poor yield of C_9F_{18}.

The isomeric C_9F_{18} fluorocarbons, which are believed to have the same carbon skeleton as the parent hydrocarbons from which they were prepared, were found to display very similar physical properties. A similar relationship existed in the C_9F_{18} series (see also Grosse and Cady, *Ind. Eng. Chem.*, 1947, **39**, 367; Fowler *et al.*, *ibid.*, p. 375), and although more refined techniques may reveal significant differences in the physical properties of these isomeric fluorocarbons, it is already apparent that the intermolecular forces in these substances are very small compared with those in normal organic compounds, whilst the intramolecular forces are very high. Fluorocarbons should, therefore, prove to be valuable for the study of the internal structure of organic molecules.

Experimental.

Apparatus.—This is represented diagrammatically in the figure. It was operated as described in Part I (*loc. cit.*).

Procedure.—The optimum conditions were determined by keeping the fluorine generation constant and investigating in turn the effect of reaction temperature, hydrocarbon addition, and nitrogen dilution of fluorine and of hydrocarbon. Unless stated otherwise, the product collected in the U tubes P was washed, dried, and distilled through an efficient fractionating column. Products collected in trap A were usually distilled separately.



f_1 *and* f_2. *Pyrex flow-meters.*
M. *Mixing chamber for fluorine and nitrogen.*
S. *Copper spiral for preheating the fluorine–nitrogen mixture.*
R. *Steel reaction vessel* (34" × 3") *filled with gold-plated copper turnings.*
T_1. *Thermometer pocket.*
B. *Nickel baffle plate, extending* ½ *length of R; lower half drilled with* $\frac{1}{16}$" *holes* ½" *apart.*
H. *Furnace for preheating hydrocarbon–nitrogen mixture.*
V. *Copper–glass ground joint.*
G. *Graduated 50-c.c. Pyrex vessel carrying a thermometer,* T_2.
F. *Silica tube furnace for heating the hydrocarbon reservoir.*
A *and* B. *Traps for the condensation of polymeric material.*
L. *Copper tube dipping into "Carechlor" or a fluorinated oil to act as a safety valve.*
K. *Potassium fluoride scrubber (removed during preparation of high-boiling fluorocarbons).*
P. *Two copper* U *tubes joined in series and cooled by a mixture of solid carbon dioxide and alcohol.*
W. *Liquid-air trap to condense any volatile decomposition products.*

Preliminary experiments were carried out with each compound to find the approximate b. p. of the required fluorocarbon. An arbitrary temperature range covering this value was adopted, and the yield of product distilling in this range was used to compare the efficiency of the various experiments. The distillate with b. p. below that of the fluorocarbon was termed "decomposition products," and that with boiling point greater than that of the fluorocarbon was termed "partially fluorinated" or "hydrofluorocarbon" material.

Benzene was fluorinated from time to time to make sure that there was no leakage in the apparatus and that the catalyst was fully active.

Results.—(A) *Fluorination of benzene.* (*a*) When benzene (added at 4 c.c./hr.) was diluted with nitrogen (10 l./hr.) and treated with fluorine (15 g./hr.) diluted with nitrogen (10 l./hr.) the optimum temperature was found to be approx. 280° by the following results:

$$\text{"Recovery"} = \frac{\text{Wt. of crude fluorocarbon (b. p. 48—58°)}}{\text{Wt. of benzene}} \times 100$$

Temp.	200°	250°	280°	300°	350°
"Recovery"	101	151	153	143	118

(*b*) With this optimum temperature (280°), a benzene addition of 4 c.c./hr. diluted with nitrogen (10 l./hr.), and a fluorine addition of 15 g./hr., the following results were obtained upon varying the dilution of fluorine with nitrogen:

N_2 Dilution of F_2 (l./hr.)	2	6	8	10	15
"Recovery"	51	90	155	153	102

These results showed that a 40% yield of perfluorocyclohexane could be produced from benzene under the following optimum conditions: temp. 280°; benzene 4 c.c./hr. diluted with 10 l. of nitrogen/hr.; fluorine, 15 g./hr., diluted with 8 l. of nitrogen/hr.

Purification of the fluorocarbon as described later gave perfluorocyclohexane, m. p. 51°, b. p. 52°, D_4^{20} 1·72 g./c.c. (Found: C, 23·8; F, 75·6%; *M*, 299. Calc. for C_6F_{12}: C, 24·0; F, 76·0%; *M*, 300). Bigelow and Fukuhara (*J. Amer. Chem. Soc.*, 1941, **63**, 2792) quote m. p. 48—49°, b. p. 50°; D^{20} 1·684 for this compound, and Christoffers, Lingafelter, and Cady (*ibid.*, 1947, **69**, 2502) give m. p. 58·2° (sealed tube), sublimes 51°/760 mm., D^{20} 1·93.

Partially fluorinated benzene. A high nitrogen dilution was found to be a major factor in forming hydrofluorocarbons. The following experiment with benzene is typical of many carried out to prepare

hydrofluorocarbons. Nitrogen (13 l./hr.) was bubbled through benzene so that the latter was carried into the reactor (adjusted to 280°) at the rate of 5·5 c.c./hr. Fluorine (15 g./hr.) diluted with nitrogen (17 l./hr.) was also introduced into the reactor. After 4 hours, the combined crude yield (28·7 g.) gave upon fractional distillation: fraction 1 (decomposition products), 8·3 g., b. p. 25—48°; fraction 2 (crude perfluorocyclohexane), 7·5 g., b. p. 48—58°; fraction 3 (partially fluorinated benzene), 10·6 g. (40% of total), b. p. 58—150°.

The partially fluorinated benzene fraction was a complex mixture which could not be separated easily into its constituents by fractional distillation. Examination of the fractions from a distillation of hydrofluorobenzene material (in which partial separation had been effected) indicated, however, that as the percentage of fluorine increased the b. p.s of the compounds steadily increased to a maximum, after which they steadily fell to a value below that of the parent hydrocarbon. Finally, a minimum value was reached when the material was completely fluorinated thus:

Fraction.	B. p.	F (%).*	*M* (Regnault method).	Fraction.	B. p.	F (%).*	*M* (Regnault method).
1	60—70°	70·4	270	3	100—110°	56·7	190
2	90—100	66·3	240	4	120—140	36·1	128

* Fluorine analyses were carried out by decomposing the fluorocarbon with potassium and precipitating the fluoride as calcium fluoride. This gave reproducible results but invariably they were slightly low. The molecular weights were usually determined in a Regnault bulb, but for compounds of high b. p. an ebullioscopic method was used.

The calculated analytical data for some partially fluorinated benzenes are as follows: $C_6H_4F_2$, F, 42·5%; *M*, 134. $C_6H_3F_3$, F, 59·4%; *M*, 192. $C_6H_2F_4$, F, 69·5%; *M*, 246. C_6F_{12}, F, 76·0%; *M*, 300. In view of the probable contamination from partially fluorinated and polymeric compounds arising from the fragmentation of the parent hydrocarbon, the correlation of the experimental analytical figures with possible empirical formulæ for hydrofluorobenzenes must be treated with reserve.

Examination of polymeric material. Distillation of the combined still residues from a series of experiments gave a range of products varying from a colourless mobile liquid (b. p. 140—160°/10 mm.) to a thick opaque oil (b. p. 200—240°/10 mm.).

(B) *Fluorination of Benzotrifluoride.*—Under the optimum conditions (temp. 200°; F_2, 13 g./hr.; benzotrifluoride addition (5 c.c./hr.; N_2 dilution of F_2, 13 l./hr.; N_2 dilution of benzotrifluoride, 10 l./hr.), benzotrifluoride (72 g.) yielded a crude product (84·1 g.) which gave upon fractional distillation: fraction 1, decomposition products, 18·7 g., b. p. 30—72°; fraction 2, perfluoromethylcyclohexane, 50·5 g. ("recovery" 70%), b. p. 72—78°; fraction 3, partially fluorinated product, 12·1 g., b. p. 78—150°.

Fractional distillation of crude fluorocarbon (117 g.) corresponding to fraction 2, followed by purification as described later, gave perfluoromethylcyclohexane (82·7 g.), b. p. 76·2°, f. p. −38°, n_D^{25} 1·276, D_4^{25} 1·784 g./c.c., γ^{25} 13·8 dynes/cm., η^{25} 15·6 millipoises (Found: C, 23·7; F, 75·5%; *M*, 347. Calc. for C_7F_{14}: C, 24·0; F, 76·0%; *M*, 350). Grosse and Cady (*loc. cit.*) give b. p. 76°, D^{20} 1·7770, n_D^{25} 1·2762, and Fowler *et al.* (*loc. cit.*) give b. p. 76·32°, D^{20} 1·7994, n_D^{25} 1·2815, γ^{20} 15·4 for this substance.

From a number of experiments it was observed that an increase in the nitrogen dilution of the hydrocarbon gave a higher yield of hydrofluorocarbon and polymeric materials.

Fractional distillation of the decomposition products, fraction 1 (b. p. 30—72°), showed that the bulk of the material had b. p. 48—60°. A pure compound could not be isolated but it is believed that the fluorocarbon, b. p. 48—60°, was mainly a mixture of perfluorocyclohexane and perfluorohexane, since the analysis of the decomposition material shows that it consists largely of completely fluorinated compounds (Found: F, 76·2%; *M*, 309. Calc. for C_6F_{12}: F, 76·0; *M*, 300. Calc. for C_6F_{14}: F 78·7%; *M*, 338).

A parallel series of experiments with toluene showed that the optimum fluorination temperature was 250°.

(C) *Fluorination of Xylene (Technical).*—The optimum conditions were found to be: temp. 200°, xylene addition 4 c.c./hr., diluted with 14 l. of nitrogen/hr.; and fluorine 15 g./hr., diluted with 9 l. of nitrogen/hr. Under these conditions xylene (40 g.) gave a product (48·8 g.) in the U-tubes from which perfluorodimethylcyclohexane (12 g.) ("recovery" 27·5%), b. p. 95—100°, was separated by fractional distillation. Purification of 101 g. of this crude fluorocarbon afforded 67 g. of perfluorodimethylcyclohexane, b. p. 101·5°, f. p. −55°, D_4^{25} 1·829, n_D^{25} 1·283, γ^{25} 15·1 dynes/cm., η^{25} 19·3 millipoises (Found: C, 24·0; F, 75·7%; *M*, 395. Calc. for C_8F_{14}: C, 24·0; F, 76·0; *M*, 400). Grosse and Cady (*loc. cit.*) give b. p. 100°, D^{20} 1·8270, n_D^{25} 1·2858; Fowler *et al.* (*loc. cit.*) record b. p. 101·5—102·4°, D^{20} 1·8530, n_D^{25} 1·2902, γ^{20} 16·3 dynes/cm. Both groups of workers believed the products to be a mixture of isomers.

Experiments were carried out on the recycling of the hydrofluorocarbon fraction (b. p. 105—170°). "Recovery" figures of 70—80% showed that good yields of fluorocarbon could be produced in this way. As with the parent hydrocarbon, the reaction temperature was found to be critical since at 250° the decomposition products amounted to 41% of the total distillate while at 200° they amounted to 20%; moreover, the perfluorodimethylcyclohexane increased from 34% at 250° to 40% at 200°.

It is noteworthy that the hydrofluorocarbon produced in these experiments underwent partial polymerisation simply on heating, as indicated by a marked increase in its b. p.

Examination of polymeric material. The fraction, b. p. >170°, from the fluorination of 414 g. of xylene was divided into two portions (*a*) and (*b*). Each was freed from an upper tarry layer by extraction with ether and then distilled. Portion (*a*) gave: fraction 1 (decomposition products, formed either on

storage or by heat during distillation), 24·3 g., b. p. 70—95°; fraction 2 (a pale yellow thin oil), 18·0 g., b. p. (bath temp.) 170—210°/10 mm.; fraction 3 (a pale yellow viscous oil), 18·0 g., b. p. (bath temp.) 210—260°/10 mm. (*M*, ebullioscopic, 620—650).

Portion (*b*) gave: fraction 1 (decomposition products), 5·7 g., b. p. 70—90°; fraction 2 (colourless thin oil), 15·7 g., b. p. (bath temp.) 100—170°/10 mm.; fraction 3 (colourless oil), 31·7 g., b. p. (bath-temp.) 170—210°/10 mm. [Found: C, 44·4; H, 2·1; F, 53·0%; *M* (ebullioscopic), 437. Calc. for $C_{10}H_2F_{12}$: C, 44·9; H, 1·9; F, 53·3%; *M*, 428]. The compounds may be dimers of partly fluorinated xylenes, *e.g.* $(CH_2{\cdot}C_6F_4{\cdot}CHF_2)_2$ or $[C_6H_4(CF_2)_2]_2$—it is evident from the molecular weight and C and F figures that the material is neither a completely fluorinated hydrocarbon nor a partly fluorinated xylene; fraction 4 (colourless viscous oil), 8·7 g., b. p. (bath temp.) 210—260°/10 mm.; fraction 5 (yellow glass), 10·0 g., b. p. (bath temp.) 260—300°/10 mm.

The difference in the products of distillation of the two samples is explained by the fact that portion (*a*) had been left for several weeks before distillation, during which time some decomposition had occurred.

The amount of oily material distilling in the range 170—210°/10 mm. was relatively large in both distillations, but in spite of repeated distillation, a definite fraction of perfluoro-oil could not be separated.

Examination of decomposition products. Refractionation of the combined decomposition products from the 414 g. of xylene gave: fraction 1, 4·0 g., b. p. 30—80°; fraction 2, 88·3 g., b. p. 85—95°; fraction 3, perfluorodimethylcyclohexane, 12·6 g., b. p. 95—105°; still residue, 5·1 g. Fraction 2, which had F, 76·1%, and an average *M* of 340, appeared to contain mainly cyclic perfluoro-compounds and perfluoroparaffins, but fractional distillation failed to give any one component.

(D) *Fluorination of* 1 : 3-*Bistrifluoromethylbenzene.*—This substance, prepared by the hydrofluorination of 1 : 3-bistrichloromethylbenzene, was fluorinated at 200°, the optimum temperature for the fluorination of xylene. The hexafluoroxylene (62 g.) was carried from a reservoir (temp. 90°) at 7 c.c./hr. in a stream of nitrogen (25 l./hr.) into the reactor at the same time that fluorine (10 g./hr.) diluted with nitrogen (16 l./hr.) was also added. Fractional distillation of the crude fluorocarbon (79·2 g.) yielded: fraction 1, (decomposition products) 15·6 g., b. p. 30—95°; fraction 2, crude perfluorodimethylcyclohexane (10·3 g.), b. p. 95—105°; fraction 3 (partly fluorinated material) (27·9 g.), b. p. 105—170°; fraction 4 (polymeric material), 11 g., b. p. >170°.

When the nitrogen dilution of the fluorine was increased from 16 to 22 l./hr. the crude yield (76·1 g. from 69 g. of starting product) was almost the same, but both the yield of decomposition product (8·2 g.) and that of crude perfluorodimethylcyclohexane (4·8 g.) fell while the yield of polymer (27 g.) increased.

Refractionation of the combined decomposition products and the crude desired fluorocarbon gave perfluoro-1 : 3-dimethylcyclohexane (14 g. or 11% of the hexafluoroxylene used). Comparison of this with the total polymer (56·2 g. or 43% of the hexafluoroxylene) showed that vapour-phase fluorination of hexafluoroxylene under the conditions specified resulted mainly in polymerisation (cf. Cady *et. al.*, *loc. cit.*).

(E) *Fluorination of* o-*Xylene.*—Only small yields of perfluoro-1 : 2-dimethylcyclohexane could be produced by fluorination of *o*-xylene at 200°. The main products were those of decomposition and partial fluorination. A decrease in the rate of addition of hydrocarbon reduced polymer formation but neither the "recovery" nor the yield of perfluorodimethylcyclohexane was improved. Redistillation of the combined fractions of perfluorodimethylcyclohexane and decomposition fragments (from 122 g. of *o*-xylene) afforded perfluoro-1 : 2-dimethylcyclohexane (4·6 g.). Although this fraction cannot be considered pure, its physical properties, b. p. 100—102°, n_D^{25} 1·285, D_4^{25} 1·825 g./c.c., corresponded closely to those of perfluoro-1 : 3-dimethylcyclohexane (Fowler *et al.*, *loc. cit.*, record b. p. 102·6°, D^{20} 1·8672, n_D^{20} 1·2923 for perfluoro-1 : 2-dimethylcyclohexane).

(F) *Fluorination of* m-*Xylene.*—By analogy with previous experiments with the xylenes (Sections C and E) the reaction temperature was adjusted to 200°. The flow of fluorine, and its dilution with nitrogen were kept fairly constant so that the effect of varying the rate of addition of xylene and its dilution with nitrogen could be ascertained. The best yields of perfluoro-1 : 3-dimethylcyclohexane were obtained when xylene was transported from the reservoir (adjusted to 105—110°) at 3—4 c.c./hr. in a stream of nitrogen (18 l./hr.). Thus *m*-xylene (77 g.) afforded 22 g. of product in traps *A* and *B* and 83·8 g. in the U-tubes. Distillation of the U-tube product gave: fraction 1, decomposition products (40 g.), b. p. 40—95°; fraction 2, crude perfluoro-1 : 3-dimethylcyclohexane (23·6 g.), b. p. 95—105°; fraction 3, hydrofluorocarbon (9·3 g.), b. p. 105—170°; fraction 4, polymeric material (1·1 g.), b. p. >170°.

Purification of fraction 2 gave rise to perfluoro-1 : 3-dimethylcyclohexane, b. p. 101·5°, f. p. −56°, D^{25} 1·829 g./c.c., n_D^{25} 1·283, γ^{25} 15·1 dynes/cm., η^{25} 19·3 millipoises (Fowler *et al.*, *loc. cit.*, record b. p. 102·12°, n_D^{25} 1·2908, D^{20} 1·8560 for this fluorocarbon). After the fluorination of 206 g. of the xylene, the reactor was dismantled, and a thick viscous colourless oil (15 g.) extracted from it and purified by distillation in high vacuum (Found: F, 74·1%). As far as viscosity, and stability to heat, fluorine, and uranium hexafluoride are concerned, this oil compared favourably with similar fluoro-oils prepared later by liquid-phase polymerisation of hydrofluorocarbons.

During the course of the experiments it was found that polymer formation was favoured by a high rate of addition of *m*-xylene.

(G) *Fluorination of Ethylbenzene.*—By following the procedure already outlined above, the optimum conditions were found to be: temp. 200°; ethylbenzene addition, 5·5 c.c./hr., diluted with 25 l. of nitrogen/hr.; fluorine, 24 g./hr., diluted with 14 l. of nitrogen/hr. Under these conditions 52 g. of ethylbenzene furnished 24·2 g. of crude perfluoro-derivative, b. p. 100—103°, which upon purification yielded *perfluoroethylcyclohexane*, b. p. 101·5°, f. p. −60°, D_4^{25} 1·826 g./c.c., n_D^{25} 1·283, γ^{25} 15·0 dynes/cm., η^{25} 19·1 millipoises (Found: F, 75·7%; *M*, 396. C_8F_{16} requires F, 76·0%; *M*, 400).

(H) *Fluorination of Mesitylene.*—Under the optimum conditions (temp. 230°; mesitylene addition 4 c.c./hr. diluted with 11 l. of nitrogen/hr.; fluorine addition 17 g./hr. diluted with 9 l. of nitrogen/hr.), 42 g. of mesitylene yielded 12·4 g. of crude perfluorocarbon, b. p. 120—128°. Purification of 63 g. of product obtained in this way gave perfluoro-1 : 3 : 5-trimethylcyclohexane, b. p. 124·6°, f. p. −56°, D_4^{25} 1·800 g./c.c., n_D^{25} 1·294, γ^{25} 17·2 dynes/cm., η^{25} 22·4 millipoises. Grosse and Cady (*loc. cit.*) give b. p. 123°, n_D^{25} 1·2930, D^{20} 1·8676, and Fowler *et al.* (*loc. cit.*) give b. p. 125·18°, n_D^{25} 1·2995, D^{20} 1·9025 for this compound (Found: C, 23·5; F, 75·8%; *M*, 443. Calc. for C_9F_{18}: C, 24·0; F, 76·0%; *M*, 450).

Considerable polymerisation took place during these experiments. Distillation of 124 g. of this material collected in traps *A* and *B* from 10 experiments gave:

Fraction.	Wt. (g.).	B. p. (bath temp.)/10 mm.	F (%).	*M* (ebull.).
1. Colourless oil	11·2	120—160°	—	—
2. Colourless viscous oil	59·1	160—210	68·2	520
3. Colourless very viscous oil	27·0	210—260	—	—
4. Colourless very viscous oil	14·2	260—300	59·7	580
5. Pale yellow glass	2·0	>300	—	—

(J) *Fluorination of φ-Cumene.*—This hydrocarbon gave poor results compared with mesitylene; considerable decomposition occurred and tar-like material as well as fluorocarbon collected in the U-tubes. Treatment of 124 g. of φ-cumene (at the rate of 4 c.c./hr. diluted with 20 l. of nitrogen/hr.) with fluorine (20 g./hr. diluted with 14 l. of nitrogen/hr.) at 230° furnished a U-tube condensate which upon distillation gave: fraction 1 (decomposition products), 19·4 g., b. p. 40—124°; fraction 2, *perfluoro-1 : 2 : 4-trimethylcyclohexane*, 5·2 g., b. p. 124—126° (Found: F, 75·6%; *M*, 445. C_9F_{18} requires F, 76·0%; *M*, 450); fraction 3, hydrofluorocarbon, 16·5 g., b. p. 126—170°. Since the perfluoro-1 : 2 : 4-trimethylcyclohexane amounting to 4% by weight of the hydrocarbon fluorinated boiled over the range 124—126°, its properties (D_4^{25} 1·881, n_D^{25} 1·296, γ^{25} 17·5 dynes/cm., η^{25} 22·5 millipoises) are quoted with reserve. It is to be noted, however, that these physical properties closely resemble those of perfluoro-1 : 3 : 5-trimethylcyclohexane.

Purification of Fluorocarbons.—The physical properties quoted above (and of which use will be made in a later communication) were determined on samples which had been washed with water, alcohol (to remove hydrofluorocarbon), water, and dried (phosphoric oxide); they were then distilled, and the fluorocarbon collected over a close range, treated with uranium hexafluoride either in a closed Pyrex vessel on a hot water-bath or by refluxing the fluorocarbon with the hexafluoride until no more green tetrafluoride was produced. The fluorocarbon was then washed, dried, and distilled through an efficient column.

The authors express their thanks to (the late) Sir Norman Haworth, F.R.S., and Professor M. Stacey, F.R.S., for their interest in this work. They also thank the Director General of Scientific Research for permission to publish.

THE CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, February 16th*, 1950.]

---

517. *The Composition of the Polysaccharide synthesised by* Polytomella cæca.

By E. J. BOURNE, M. STACEY, and I. A. WILKINSON.

Polytomella cæca synthesises a starch from ethyl alcohol or acetic acid as the source of carbon. The starch is best separated from proteins and other cellular components with chloral hydrate solution. It contains 13—16% of amylose and 84—87% of amylopectin. *Polytomella cæca* may well be a convenient organism for the production of an enzyme capable of synthesising branched polysaccharides of the amylopectin–glycogen class.

IN a recent communication (*Biochim. Biophys. Acta*, 1950, **4**, 270) Lwoff, Ionesco, and Gutmann reported that *Polytomella cæca*, a flagellate not containing chlorophyll, synthesises during its growth a relatively large amount of a granular starch, which gives a purple stain with iodine. They observed that, whereas the organism grows rapidly on a synthetic medium containing ammonium sulphate as the nitrogen source and acetic acid or ethyl alcohol as the carbon source, it is unable to utilise sugars such as glucose, maltose, sucrose, and trehalose. The French workers obtained evidence that the immediate precursor of the starch is glucose-1 phosphate and that this ester is converted into the polysaccharide by the agency of phosphorylase.

Since it is now generally agreed that phosphorylases isolated from plant and animal sources convert the Cori ester into linear polyglucoses of the amylose type, and that a supplementary enzyme is necessary for the synthesis of branched structures of the amylopectin–glycogen class (for summaries see Cori, Swanson, and Cori, *Fed. Proc.*, 1945, **4**, 234; Bernfeld and Meutémédian, *Helv. Chim. Acta*, 1948, **31**, 1724, 1735; Barker, Bourne, Wilkinson, and Peat, *J.*, 1950, **93**), it is of interest to know whether the starch of *Polytomella cæca* contains amylopectin and hence

whether the organism might be expected to yield an enzymic branching factor. Through the courtesy of Dr. Lwoff we have been able to examine his culture of *Polytomella cœca* and the starch which it synthesises. We now furnish evidence that this starch is composed of both amylose and amylopectin and is indeed richer in the latter component than are most natural starches.

On microscopical examination it can be seen that individual *Polytomella* organisms contain starch grains, which are much smaller than those of potato starch but which, nevertheless, can be identified easily under the microscope. The organism can be ruptured very readily by mechanical means, even by centrifuging at high speeds, with release of the starch grains. The sediment consists mainly of starch, together with small amounts of minerals, proteins, and other cellular debris. A sample of starch prepared in this way from alcohol and sodium acetate as the carbon source was kindly supplied by Dr. Lwoff; this will be referred to below as "untreated starch."

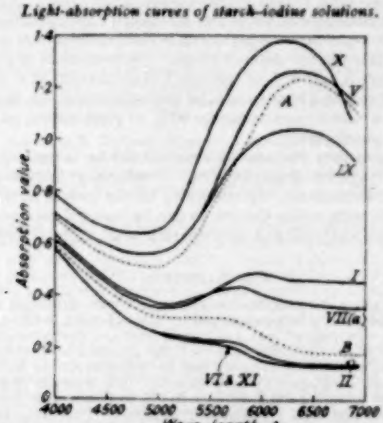
When a portion of the untreated starch was boiled with water and centrifuged, three distinct layers were obtained, namely, a clear solution at the top, a turbid viscous solution in the centre, and a light brown solid at the bottom. The addition of alcohol to the separated aqueous layers precipitated fractions I (45·4%) and II (22·0%), respectively. The light brown solid was sub-divided by extraction with hot alkali into a soluble portion (fraction III; 14·1%) and an insoluble portion (fraction IV; 5·0%). Neither of these alkali-treated fractions was soluble in water and so they could not be submitted to the usual diagnostic tests for amylose and amylopectin; they contained the whole of the protein present in the untreated starch.

TABLE I.

Characteristics of starch fractions I—VI.

Fraction.	I.	II.	III.	IV.	V.	VI.
Yield (%) from untreated starch	45·4	22·0	14·1	5·0	12·3	30·6
Ash (%)	0·4	1·6	2·5	13·9	0·0	1·3
Protein tests	−ve	−ve	+ve	+ve	−ve	−ve
Conversion (%) into glucose by acid	98	94	90	72	99	98
B.V.	0·46	0·14	—	—	1·18	0·13
Limiting conversion (%) into maltose with β-amylase	68	—	—	—	89	52

Light-absorption curves of starch–iodine solutions.



A = Potato amylose } *Typical samples prepared by the thymol method (cf. Bourne, Dounison, Haworth, and Peat,* loc. cit.).
B = Potato amylopectin }

In its blue value and in its limiting conversion into maltose with β-amylase (see Table I and Fig.), fraction I closely resembled potato starch, whereas fraction II was similar to potato amylopectin and to waxy-maize starch (cf. Barker, Bourne, and Peat, *J.*, 1949, 1712). Thus

it is reasonable to suppose that the whole of the amylose component of the untreated starch had been isolated in fraction I, the fraction most readily dispersed in boiling water. By selective precipitation with thymol, fraction I was separated into its linear (V) and branched (VI) constituents (cf. Bourne, Donnison, Haworth, and Peat, *J.*, 1948, 1687). The amylose component represented 27·0% of fraction I, corresponding to 12·3% of the untreated starch.

TABLE II.

Characteristics of starch fractions VII(*a*)—XI.

Fraction.	VII(*a*).	VIII.	IX.	X.	XI.
Yield (%) from untreated starch	88·9	7·3	16·9	14·1	65·4
Ash (%)	0·8	17·4	1·4	—	0·0
Protein tests	−ve	+ve	−ve	−ve	−ve
Conversion (%) into glucose by acid	94	55	93	—	92
B.V.	0·36	—	0·96	1·13	0·11
Limiting conversion (%) into maltose with β-amylase	54	—	71	89	48
$[\alpha]_D^{20}$ in 0·5*N*-sodium hydroxide	+160°	—	—	—	—

A more convenient and more efficient method for the purification of the untreated starch proved to be that of exhaustive extraction with an aqueous solution of chloral hydrate (cf. Meyer and Bernfeld, *Helv. Chim. Acta*, 1940, **23**, 875). A control experiment revealed that this treatment had a negligible effect upon the blue value of potato starch. Approximately 90% (fraction VII) of the untreated *Polytomella cæca* starch was recovered from the chloral hydrate solution; it was free from protein and contained only a trace of mineral matter. The material which was insoluble in the chloral hydrate solution (fraction VIII) was rich in both proteins and minerals. Thus fraction VII can be regarded as virtually pure *Polytomella cæca* starch. Its physical nature was such that it did not disperse in boiling water and exhibited a strong tendency to form swollen lumps in alkali. It was rendered readily soluble in dilute alkali by slowly adding, with vigorous stirring, water and then alkali to a hot alcoholic suspension and precipitating the starch [fraction VII(*a*)] by adding alcohol to the resulting solution.

Chromatographic analysis of a hydrolysate of fraction VII(*a*) by the filter-paper method revealed one aldose spot and no ketose spots; the aldose spot corresponded to a reference glucose spot. The blue value and the β-amylolysis limit of fraction VII(*a*) indicated that it contained somewhat less amylose than does potato starch (Table II and Fig.). Confirmation of this was afforded when the polysaccharide was subjected to selective precipitation with thymol, for the precipitated fraction (IX) represented only 19%. The material not precipitated by thymol (fraction XI) had the characteristics of amylopectin. Retreatment of fraction IX with thymol yielded an amylose [fraction X; 15·8% of fraction VII(*a*)] having B.V. 1·13 and giving 89% of maltose with β-amylase. From this result and that quoted above it can be seen that the untreated *Polytomella cæca* starch contained approximately 90% of pure starch, of which about 13—16% was amylose and the rest amylopectin.

In view of these observations *Polytomella cæca* should be a fruitful source of a branching factor responsible for the synthesis of amylopectin. Preliminary indications that this is so have been obtained already. Furthermore, the simplicity of the carbon source, the rapid growth of mass cultures, and the ease with which the starch can be isolated commend *Polytomella cæca* for the synthesis of ^{14}C-labelled amylose and amylopectin and of the carbohydrates which can be derived therefrom.

EXPERIMENTAL.

Analysis of Starch Fractions.—All polysaccharide samples were dried for several hours at 60° in a vacuum over phosphoric oxide before being analysed by the following methods: (a) *Ash content.* The polysaccharide (12—15 mg.) was weighed into a platinum boat and heated to constant weight in a small muffle furnace. (b) *Protein tests.* In order to detect the presence of proteinaceous impurities, each starch fraction was submitted to the sodium fusion test for nitrogen and to Millon's mercuric nitrite test for phenolic amino-acids. (c) *Hydrolysis by aqueous acid.* The amount of glucose formed when the polysaccharide was heated in a boiling water-bath with 7% sulphuric acid for 6 hours was determined by cuprimetric titration, as described by Bourne, Donnison, Haworth, and Peat (*loc. cit.*). (d) *β-Amylolysis.* The limiting conversion into maltose effected by soya-bean β-amylase at pH 4·8 was determined by the method of Bourne, Donnison, Haworth, and Peat (*loc. cit.*). (e) *Iodine stains.* Two expressions, absorption value (A.V.) and blue value (B.V.), are used in this paper to describe the intensities of the iodine stains of polysaccharides; they were defined by Bourne, Haworth, Macey, and Peat (*J.*, 1948, 924). Since the B.V. is determined under standard conditions (polysaccharide, 1 mg./100 c.c.; iodine, 2 mg./100 c.c.; potassium iodide, 20 mg./100 c.c.) and at λ 6800 A., it is characteristic of the polysaccharide under examination. On the other hand, the A.V. is a convenient term for an absorption measurement made under any given set of conditions.

Untreated Starch from Polytomella cœca.—The untreated starch employed in these investigations had been isolated from a mass culture of *Polytomella cœca*. Details of the growth of such a mass culture, in which alcohol and sodium acetate serve as the carbon source, were given by Lwoff, Ionesco, and Gutmann (*loc. cit.*). This starch, which contained protein (4·1%) and mineral matter (2·3% ash), was only partially dispersed in boiling water.

Extraction of the Untreated Starch with Boiling Water and with Alkali.—A suspension of the finely-ground untreated starch (dry weight, 1·925 g.) in alcohol (20 c.c.) was stirred into boiling water (200 c.c.). The paste was boiled and stirred for 35 minutes, cooled, and centrifuged; three distinct layers were formed: between the bottom layer of light-brown solid and the clear aqueous upper solution was a turbid viscous layer.

The top layer was mixed with alcohol (1·5 vols.) and the precipitated polysaccharide was collected. It was ground thoroughly with alcohol and then with ether, and finally dried at 60° in a vacuum over phosphoric oxide, giving fraction I (0·873 g.; 45·4%). In the same way, fraction II (0·422 g.; 22·0%) was recovered from the central viscous layer.

The light brown residue was extracted, at 50°, with three portions (20 c.c. each) of 0·25*N*-sodium hydroxide. The extracts were combined, neutralised to phenolphthalein with hydrochloric acid, and dialysed in Cellophane against distilled water. The polysaccharide was precipitated from solution with alcohol (1·5 vols.), and washed and dried as above, to give fraction III (0·272 g.; 14·1%).

The alkali-insoluble material was washed with a small volume of water, ground with alcohol and then with ether, and dried as above, to give fraction IV (0·096 g.; 5·0%).

Extraction of the Untreated Starch with Chloral Hydrate Solution.—The method employed was essentially that reported by Meyer and Bernfeld (*loc. cit.*). The untreated starch (dry weight, 2·00 g.) was stirred at 80° for 1 hour with a 33% solution (100 c.c.) of chloral hydrate in water. The insoluble residue, which was collected in the centrifuge, was stirred with two fresh portions (20 c.c. each) of warm chloral hydrate solution.

The combined extracts were filtered through sintered glass and injected in a fine stream into acetone (250 c.c.). The flocculent polysaccharide was collected and hardened by trituration with acetone. The last traces of chloral hydrate were removed by extraction in a Soxhlet apparatus with acetone for 2 hours and then with ether for 1 hour. The purified product (fraction VII; 1·778 g.; 88·9%) was dried as above.

The material insoluble in chloral hydrate, when washed repeatedly with acetone and then with ether and dried as above, constituted fraction VIII (0·146 g.; 7·3%).

Reprecipitation of Fraction VII.—As obtained above, fraction VII consisted of hard granules, which, owing to their insolubility in water and their tendency to form gelatinous lumps in alkali, were unsuitable for quantitative measurements. After the following treatment, it was recovered in a form which was readily soluble in dilute alkali.

Fraction VII, suspended in a small volume of alcohol, was heated in a boiling water-bath and stirred at high speed while water (150 c.c. per 1 g. polysaccharide) was added. The stirring and heating were continued for 20 minutes. At this stage most of the polysaccharide had dissolved, the rest remaining as a very fine suspension. The addition of a few drops of 10% sodium hydroxide solution caused rapid completion of the solution process. After 5 minutes, the solution was allowed to cool and was then neutralised with hydrochloric acid. The polysaccharide was precipitated with alcohol (1·5 vols.), triturated with alcohol and then with ether, and dried as above to give fraction VII(*a*), having $[\alpha]_D^{25}$ + 160° (*c*, 0·19 in 0·5*N*-sodium hydroxide).

Extraction of Potato Starch with Chloral Hydrate Solution.—Potato starch (B.V. 0·42; 2·00 g.) dissolved completely when treated with chloral hydrate solution (100 c.c.), as described above. The polysaccharide was precipitated from the viscous solution with acetone, purified, and dried. The product had B.V. 0·41. Thus the effect of this treatment on the B.V. of either amylose or amylopectin is negligible.

Characterisation of Fraction VII(a) *as a Polyglucose.*—A portion (40 mg.) of fraction VII(*a*) was hydrolysed for 5 hours with 2*N*-sulphuric acid (1·0 c.c.) in a sealed tube which was heated in a water-bath at 100°. The hydrolysate and water washings (1·0 c.c.) were transferred to a small centrifuge tube, neutralised with barium carbonate, and centrifuged. The supernatant liquid, in which the concentration of sugars was approximately 2%, was analysed chromatographically on filter paper by the method of Partridge (*Nature*, 1946, **158**, 270). Five reference solutions were employed, namely, glucose (0·1%), galactose (0·1%), fructose (0·1%), sucrose (0·1%), and a mixture of these four sugars (0·1% each).

Spots of the hydrolysate and of each of the five reference solutions were applied along a line drawn 10 cm. from the top edge of each of two sheets (A and B; 57 × 23 cm.) of Whatman No. 1 filter-paper. A pad of cotton-wool was fastened to the lower edge of each sheet to absorb the solvent as it reached the bottom, and thus to enable the sugars to travel a greater distance (cf. Miettinen and Virtanen, *Acta Chem. Scand.*, 1949, **3**, 459). The sheets were irrigated for 72 hours at 15—18° with the butanol phase of a mixture of *n*-butanol (400 c.c.), ethanol (100 c.c.), ammonia (10 c.c.; *d* 0·880), and water (490 c.c.). After being dried in a current of warm air, sheet A was sprayed with aniline hydrogen phthalate reagent (Partridge, *Nature*, 1949, **164**, 443), while sheet B was sprayed with an acid resorcinol reagent.

Sheet B showed no spots other than the reference spots of sucrose and fructose, indicating that no ketose constituted more than 5% of the monosaccharide units in fraction VII(*a*). Sheet A showed a small but distinct separation of the reference aldoses, glucose and galactose; the hydrolysate of fraction VII(*a*) gave only one spot, and this corresponded to the reference glucose spot. Thus it is probable that no aldose, other than glucose, constituted more than 5% of the monosaccharide units in fraction VII(*a*).

Treatment of the Polysaccharides with Thymol.—A solution of the polysaccharide in 0·5*N*-sodium hydroxide (2 c.c. per 100 mg.) was diluted with water (35 c.c. per 100 mg.) and neutralised with 0·5*N*-sulphuric acid. Powdered thymol (0·2 g. per 100 mg. of polysaccharide) was added, and the mixture kept at 30° for 36 hours.

The precipitated polysaccharide–thymol complex was removed by the centrifuge and washed twice with saturated thymol-water, the washings being added to the original supernatant liquid. The amylose complex was washed thoroughly with absolute alcohol and then with ether, and the residual polysaccharide was dried to constant weight in a vacuum over phosphoric oxide. The soluble polysaccharide was precipitated from the aqueous solution with alcohol, washed, and dried.

The authors express their gratitude to Dr. A. Lwoff, of the Institut Pasteur, for providing the starch used in this investigation, and to Messrs. Courtaulds' Scientific Trust for financial assistance to one of them (I. A. W.). The expenses were defrayed by a grant from Imperial Chemical Industries Ltd.

THE UNIVERSITY, EDGBASTON, BIRMINGHAM 15. [*Received, May 26th*, 1950.]

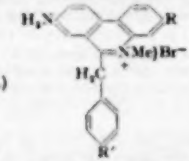
---

518. *Potential Trypanocides of the N-Heterocyclic Series. Part IV. 9-Benzoyl- and 9 : 10-Dihydro-phenanthridines.*

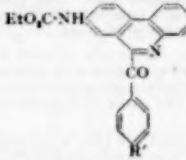
By A. G. CALDWELL, F. C. COPP, and L. P. WALLS.

7-Carbethoxyamino-9-*p*-nitrobenzoylphenanthridine (II; R = H, R′ = NO_2) was obtained by selenium dioxide oxidation of the corresponding 9-benzylphenanthridine. Reduction of its quaternary salt (III) with ferrous hydroxide gave the corresponding amino-phenanthridinium salt (V), but the iron–water method unexpectedly gave 7-carbethoxyamino-9-*p*-aminobenzoyl-10-methyl-9 : 10-dihydrophenanthridine (VIII). This anomalous reduction also occurred with 2 : 7-biscarbethoxyamino-9-benzoyl-10-methylphenanthridinium chloride. Catalytic reduction reduces other phenanthridinium salts to the 9 : 10-dihydrophenanthridines, several of which are readily converted into quaternary salts (XIII). The 9-benzoyl compounds have much feebler trypanocidal properties than the corresponding 9-phenyl compounds. The quaternary salts (XIII) are inactive.

EARLIER work in this series has established the importance, for trypanocidal activity, of the nature of the 9-substituent in phenanthridinium salts. The inactivity of the 9-*p*-aminobenzyl compound (I; R = H, R′ = NH_2) (Caldwell and Walls, *J.*, 1948, 188) might have been due to its spatial configuration, but the subsequent discovery (*J.*, 1950, 62) that the 9-benzyl analogue (I; R = NH_2, R′ = H) of Dimidium bromide is highly active renders this unlikely. The corresponding benzoyl salts (VI) and (X) have now been prepared. In the former of this pair, as in the 9-*p*-aminobenzyl compound, the possibility of additional ionic resonance between the amino-group of the 9-substituent and the hetero-N-atom is excluded.



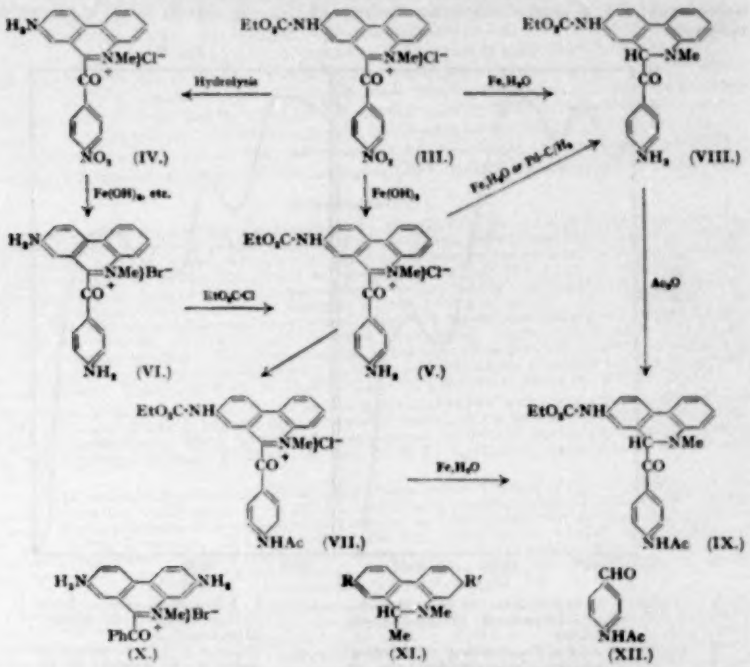
(I.)



(II.)

7-Carbethoxyamino-9-*p*-nitrobenzoylphenanthridine (II; R = H, R′ = NO_2) was obtained in 70% yield by selenium dioxide oxidation of the corresponding benzyl compound (*J.*, 1948, 191), and converted into the quaternary salt (III) by the nitrobenzene–methyl sulphate method. Hydrolysis then yielded the nitroamino-salt (IV), but reduction of (III) and (IV) to the corresponding amino-salts presented some difficulty (see chart). The desired products, (V) and (VI) respectively, were eventually obtained in good yield by the ferrous hydroxide method (*J.*, 1950, 41). The *p*-amino-group of these amino-salts reacts differently from that of the analogous 9-*p*-aminophenyl compounds; an aqueous solution of (V) was unaffected by ethyl chloroformate (Walls, *J.*, 1946, 1031) and, in spite of the presence of a free amino-group, addition of hydrochloric acid precipitated it unchanged. Likewise only one amino-group of (VI) reacted in aqueous solution with ethyl chloroformate with formation of (V) which, however, did give an acetyl derivative (VII) with acetic anhydride. The biscarbethoxyamino-salt (VII; NH·CO_2Et for NHAc) was obtained by oxidation of 7-carbethoxyamino-9-*p*-carbethoxy-aminobenzylphenanthridine (see Experimental section) with selenium dioxide to (II; R = H, R′ = NH·CO_2Et), and reaction of the product with methyl sulphate.

The iron–water method of reduction, which has been successfully used for the reduction of nitro-groups in a wide range of quaternary salt in this series, behaved anomalously with 7-carbethoxyamino-9-*p*-nitrobenzoyl-10-methylphenanthridinium chloride (III), the product being a crystalline base which did not melt sharply even after recrystallisation. On acetylation it gave a characteristic orange-red acetyl derivative, which also did not melt sharply. It seemed likely that both the nitro-group and the 9 : 10-double bond of (III) had been reduced to yield (VIII), and this explanation was supported by the following evidence. The amino-salt (V), as obtained by the ferrous hydroxide method, was converted by iron–water into an insoluble base, yielding the same acetyl derivative (IX), which was also obtained by iron–water reduction of the salt (VII). In the presence of palladium–charcoal catalyst and sodium acetate (see below) the amino-salt (V) absorbed one molecule of hydrogen, giving the same product, again identified as the acetyl derivative (IX). A 9 : 10-dihydrophenanthridine of this structure would

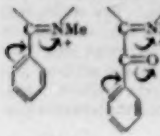


be expected to exhibit light absorption corresponding to the sum of the absorptions of its two chromophores (on the assumption that the effect of their interaction is small; cf. Braude, *J.*, 1949, 1902). In fact, the ultra-violet light absorption of the acetyl derivative (IX) is closely similar to that calculated for an equimolecular mixture of 7-acetamido-9 : 10-dimethyl-9 : 10-dihydrophenanthridine (XI; R = NHAc, R′ = H) (see below) and *p*-acetamidobenzaldehyde (XII) (Fig. 1).

For the preparation of the related series, 2 : 7-biscarbethoxyamino-9-benzoylphenanthridine (II; R = NH·CO_2Et, R′ = H) was obtained by selenium dioxide oxidation of the corresponding benzyl compound (*J.*, 1950, 62). The quaternary salt derived from it was hydrolysed to the diamino-salt (X) and readily reduced by iron–water to 2 : 7-biscarbethoxyamino-9-benzoyl-10-methyl-9 : 10-dihydrophenanthridine. The structure of this compound was confirmed by comparison of its ultra-violet light absorption with that of an equimolecular mixture of 2 : 7-bis-

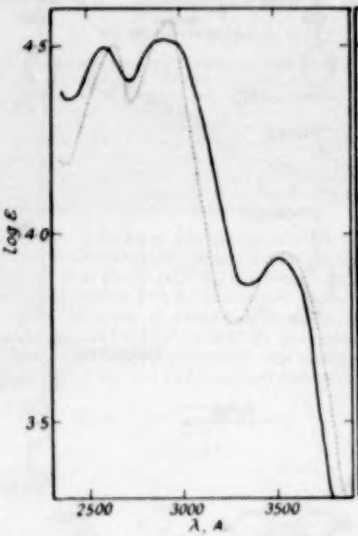
carbethoxyamino-9 : 10-dimethyl-9 : 10-dihydrophenanthridine (XI; R = R′ = NH·CO_2Et) (see below) and benzaldehyde (Fig. 2).

It is clear that the 9-benzoylphenanthridinium salts are more susceptible to certain reducing agents than are the 9-phenyl salts, and this difference may be interpreted as follows. In the 9-phenylphenanthridinium salts the polarity of the C=NMe system tends to be reduced by



electron transfer from the phenyl group, whereas in the 9-benzoyl salts this effect is reduced by the presence of the carbonyl group, which operates in the opposite sense, so that the above system is in a more highly polarised state and consequently more susceptible to attack by nascent hydrogen (see inset). This difference in behaviour to reducing agents may well affect the relationship of these salts towards enzyme systems concerned with oxidation and reduction, and it is of interest that (VI) is almost completely inactive and (X) only slightly active in trypanosome infections.

FIG. 1.



——— 7-*Carbethoxyamino*-9-p-*acetamido*-*benzoyl*-10-*methyl*-9 : 10-*dihydrophenanthridine*.
– – – – – *Mixture of* 7-*acetamido*-9 : 10-*dimethyl*-9 : 10-*dihydrophenanthridine and* p-*acetamidobenzaldehyde*.

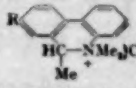
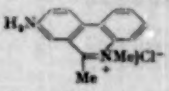
FIG. 2.

——— 2 : 7-*Biscarbethoxyamino*-9-*benzoyl*-10-*methyl*-9 : 10-*dihydrophenanthridine*.
– – – – – *Mixture of* 2 : 7-*biscarbethoxyamino*-9 : 10-*dimethyl*-9 : 10-*dihydrophenanthridine and benzaldehyde*.

Although, in general, phenanthridinium salts are unaffected by iron–water, they are readily converted into dihydro-compounds by catalytic hydrogenation in aqueous or alcoholic solution at room temperature and pressure in the presence of palladium–charcoal and a weak alkali such as sodium acetate. Reduction is more rapid with Adams's catalyst, but in the absence of other susceptible groups ceases when one molecule of hydrogen has been absorbed, even under pressure. The reduction of phenanthridine methiodide to 10-methyl-9 : 10-dihydrophenanthridine by tin and hydrochloric acid has also been reported (Ankersmit, Diss., Berne, 1891).

A series of 9 : 10-dihydrophenanthridines was prepared by this catalytic reduction method in the hope that on parenteral injection in oil into infected animals they would be oxidised by the host to the trypanocidal phenanthridinium salts from which they were derived, but would show

modified properties. They crystallise rather poorly and it was not possible to obtain pure substances from aminophenanthridinium salts, the class to which the powerful (*Trypanosoma congolense*) trypanocides belong, but 2 : 7-biscarbethoxyamino-9 : 10-dimethylphenanthridinium methyl sulphate and 3-carbethoxyamino-9-*p*-carbethoxyaminophenyl-10-methylphenanthridinium chloride, which are active against the resistant *T. cruzi* (Browning, Calver, Leckie, and

(XIII.)   (XIV.)

Walls, *Nature*, 1946, **157**, 263), readily gave crystalline dihydro-compounds. From the appropriate quaternary salts were also obtained 9 : 10-dihydro-compounds (see Table I) with methyl, phenyl, and benzyl groups in the 9-position, and similar compounds with acetamido- (XI; R = NHAc, R′ = H), carbethoxyamino- (XI; R = NH·CO_2Et, R′ = H; and R = R′ = NH·CO_2Et), hydroxy- (XI; R = OH, R′ = H), ethylcarbonato- (XI; R = O·CO_2Et, R′ = H), and methoxy-groups in the phenanthridine nucleus. Compounds of this series usually show an intense blue fluorescence in neutral or alkaline solution (Pictet and Ankersmit, *Annalen*, 1891, **266**, 138). Most of these dihydro-compounds were readily converted into non-fluorescent quaternary salts (compare XIII), which do not show promising pharmacological or therapeutic properties. 7-Acetamido-9 : 10 : 10-trimethyl-9 : 10-dihydrophenanthridinium chloride (XIII; R = NHAc) was hydrolysed to the corresponding amino-chloride hydrochloride (as XIII; R = NH_2), but this salt in contrast to the analogous (XIV) is devoid of trypanocidal properties.

Experimental.

7-Carbethoxyamino-9-p-nitrobenzoylphenanthridine.—A solution of 7-carbethoxyamino-9-*p*-nitrobenzylphenanthridine (5 g.) and selenium dioxide (1·5 g.) in dioxan (120 ml.) and water (5 ml.) was heated under reflux for 6½ hours, during which period the solution became deep red and selenium separated. The filtered solution on cooling deposited a bulky orange precipitate (2·5 g.), m. p. 242—243°. The mother-liquor was evaporated to dryness and the residue extracted with boiling benzene. The extract (charcoal) on evaporation to small bulk furnished a further 1·2 g. of product, m. p. 240—242°. On crystallisation from acetone, the pure *ketone* was obtained as a voluminous mass of fine orange needles, m. p. 243—244° (Found: C, 66·3; H, 4·2; N, 10·05; OEt, 10·85. $C_{23}H_{17}O_5N_3$ requires C, 66·5; H, 4·15; N, 10·1; OEt, 10·85%). The *oxime*, prepared by refluxing the ketone with hydroxylamine hydrochloride in pyridine solution, crystallised from methanol in small almost colourless needles, m. p. 235° (decomp.) (Found: C, 64·3; H, 4·75; N, 13·25. $C_{23}H_{18}O_5N_4$ requires C, 64·15; H, 4·2; N, 13·05%).

Hydrolysis of the urethane (1 g.) by heating for 20 minutes at 150° with concentrated sulphuric acid (2·8 ml.) and water (2·5 ml.), followed by dilution with water and neutralisation, yielded *7-amino-9-p-nitrobenzoylphenanthridine*, which crystallised from aqueous pyridine in fine dull-red matted needles, m. p. 280° (decomp.) (Found: C, 70·45; H, 4·0; N, 12·4. $C_{20}H_{13}O_3N_3$ requires C, 69·95; H, 3·8; N, 12·25%).

7-Carbethoxyamino-9-p-nitrobenzoyl-10-methylphenanthridinium Chloride (III).—A solution of the foregoing ketone (5 g.) in nitrobenzene (40 ml.) was treated with methyl sulphate (2·5 ml.) at 160°. After 3 minutes at this temperature more methyl sulphate (2·5 ml.) was added, and the temperature held at 160° for a further 5 minutes. The deep yellow solid that crystallised on cooling was collected and extracted with hot water. Addition of sodium chloride to the extract precipitated the *chloride* (3·8 g.), which crystallised from water or alcohol in small yellow needles, m. p. 237—238° (Found: C, 61·75; H, 4·7; N, 9·3; Cl, 7·8. $C_{24}H_{20}O_5N_3Cl$ requires C, 61·85; H, 4·35; N, 9·0; Cl, 7·6%).

7-Carbethoxyamino-9-p-aminobenzoyl-10-methylphenanthridinium Chloride (V).—The foregoing carbethoxyamino-nitro-salt (3 g.) in water (200 ml.) was reduced by a suspension of ferrous hydroxide, prepared by mixing solutions of crystalline ferrous sulphate (12·9 g.) in water (150 ml.) and barium hydroxide (14·1 g.) in water (150 ml.). After a few minutes' warming on the steam-bath the dark-brown precipitate was removed by filtration, and on cooling, the filtrate deposited *7-carbethoxyamino-9-p-aminobenzoyl-10-methylphenanthridinium chloride* (2·3 g.) as long fibrous, deep yellow needles, m. p. 198° (decomp.) (Found: N, 9·55; Cl, 7·75. $C_{24}H_{22}O_5N_3Cl$ requires N, 9·65; Cl, 8·15%). The *acetyl* derivative (VII), prepared by warming this amino-salt with glacial acetic acid and acetic anhydride, crystallised from water in light yellow micro-needles, m. p. *ca.* 288° (decomp.) (Found: N, 8·65; Cl, 7·25. $C_{26}H_{24}O_6N_3Cl$ requires N, 8·8; Cl, 7·45%).

7-Amino-9-p-nitrobenzoyl-10-methylphenanthridinium Chloride (IV).—A solution of 7-carbethoxyamino-9-*p*-nitrobenzoyl-10-methylphenanthridinium chloride (1 g.) in concentrated sulphuric acid (2·8 ml.) and water (2·5 ml.) was heated at 150° for 20 minutes, and then diluted with water. The maroon-coloured precipitate was collected and dissolved in water. After neutralisation with 2*N*-ammonium hydroxide, barium chloride was added to the hot solution; on cooling, the filtered solution deposited the *amino-nitro-chloride* in deep-red needles, m. p. 175° (decomp.) (Found: N, 10·8; Cl, 9·0. $C_{21}H_{16}O_3N_3Cl$ requires N, 10·65; Cl, 9·0%).

7-Amino-9-p-aminobenzoyl-10-methylphenanthridinium Bromide (VI).—7-Carbethoxyamino-9-*p*-aminobenzoyl-10-methylphenanthridinium chloride was similarly hydrolysed by sulphuric acid. After dilution with water, the clear red solution was neutralised with 2*N*-ammonium hydroxide and the *diamino-*

TABLE I.

10-*Methyl*-9 : 10-*dihydrophenanthridines*.

No.	Compound.	Solvent for crystn.	Form and m. p.	Formula.	Analyses. Found, %. C.	H.	N.	Required, %. C.	H.	N.
1	9-*Phenyl*-	Petroleum (b. p. 60—80°)	Prisms, 102—103°	$C_{19}H_{17}N$	88·95	6·45	5·05	88·55	6·25	5·15
2	9-*Benzyl*-, *hydrochloride*	EtOH	,, 175—177	$C_{21}H_{20}NCl$	78·0	6·3	— (Cl, 11·3)	78·3	6·3	— (Cl, 11·0)
3	9-p-*Methoxybenzyl*-, *hydrochloride*	,,	,, 168	$C_{22}H_{22}ONCl$	75·6	6·4	4·1	75·1	6·3	4·0
4	7-*Methoxy*-9-p-*methoxyphenyl*-	MeOH	,, 94	$C_{26}H_{21}O_2N$	80·0	6·5	4·4	79·7	6·4	4·2
5	7-*Ethylcarbonato*-9-*methyl*-	,,	,, 90	$C_{18}H_{19}O_2N$	73·3	6·5	—	72·7	6·4	—
6	7-*Hydroxy*-9-*methyl*-	,,	,, 182	$C_{14}H_{13}ON$	80·3	6·9	—	80·0	6·7	—
7	7-*Acetoxy*-9-*methyl*-	,,	,, 110—111	$C_{16}H_{15}O_2N$	76·5	6·1	—	76·4	6·4	—
8	7-*Acetamido*-9-*methyl*-	,,	,, 172—173	$C_{16}H_{16}ON_2$	76·6	6·3	10·3	76·65	6·85	10·5
9	7-*Amino*-9-*methyl*-	—	Glass, 100/10^{-3} mm. (bath temp.)	$C_{14}H_{14}N_2$	—	—	12·6	—	—	12·5
10	7-*Carbethoxyamino*-9-*methyl*-, *hydrochloride*	2N-HCl	Plates, 199 (decomp.)	$C_{18}H_{21}O_2N_2Cl$	(Cl, 10·75)		8·75	(Cl, 10·7)		8·45
11	2 : 7-*Diacetamido*-9-*phenyl*-	EtOH	Buff prisms, 184—186	$C_{22}H_{21}O_2N_3$	—	—	11·0	—	—	10·9
12	2 : 7-*Biscarbethoxyamino*-9-*methyl*-	C_6H_6–petroleum, (b. p. 60—80°)	Prisms, 169—171 (efferv.)	$C_{21}H_{24}O_4N_2$	66·2	6·7	11·0	65·75	6·6	10·95
13	3-*Carbethoxyamino*-9-p-*carbethoxyaminophenyl*-	$COMe_2$	165—170 (decomp.)	$C_{24}H_{27}O_4N_3$	70·1	5·9	10·0	70·1	6·1	9·45

The dihydro-compounds, except where otherwise stated, were obtained from the corresponding phenanthridinium salts, some of which are described in this paper and the others as follows: (2)—(4), (6), *J.*, 1950, 311. (9), (10), (12), Walls, *J.*, 1947, 71. (11), *J.*, 1945, 299. (13), *J.*, 1946, 1033.

TABLE II.

10 : 10-*Dimethyl*-9 : 10-*dihydrophenanthridinium salts*.

Compound.		Solvent for crystn.	Form and m. p.	Formula.	Analyses. Found, %. C.	H.	N.	Cl or I.	Required, %. C.	H.	N.	Cl or I.
9-*Phenyl*-	*iodide*	H_2O	Needles, 162—164° (decomp.)	$C_{21}H_{20}NI$	—	—	3·3	30·9	—	—	3·4	30·75
9-*Benzyl*-	*iodide*	EtOH	Prisms, 174—175	$C_{22}H_{22}NI$	61·8	5·4	3·5	—	61·8	5·2	3·3	—
	chloride	PrⁱOH–$COMe_2$	,, 173	$C_{22}H_{22}NCl$	78·9	6·6	4·4	10·5	78·65	6·6	4·2	10·6
9-p-*Methoxybenzyl*-	*iodide*	EtOH	Prisms, 166	$C_{23}H_{24}ONI$	60·2	5·5	—	—	60·4	5·3	—	—
	chloride	,,	,, 159	$C_{23}H_{24}ONCl$	—	—	4·1	10·3	—	—	3·8	9·7
7-*Methoxy*-9-p-*methoxyphenyl*-	*iodide*	MeOH	Plates, 169	$C_{27}H_{24}O_2NI$	58·4	5·7	3·2	—	58·3	5·1	3·0	—
7-*Ethylcarbonato*-9-*methyl*-	*iodide*	EtOH–Et_2O	Prisms, 154	$C_{19}H_{20}O_3NI$	51·9	5·15	—	—	51·95	5·05	—	—
7-*Hydroxy*-9-*methyl*-	*iodide*	H_2O	Needles, 143—144	$C_{14}H_{14}ONI$	—	—	—	34·65	—	—	—	34·6
7-*Acetoxy*-9-*methyl*-	*iodide*	EtOH–Et_2O	Prisms, 155	$C_{16}H_{16}O_2NI$	52·8	5·3	—	31·25	52·8	4·9	—	31·0
7-*Carbethoxyamino*-9-*methyl*-	*iodide*	H_2O	Prisms, 176—177 (decomp.)	$C_{18}H_{21}O_2N_2I$	—	—	6·4	28·95	—	—	6·4	29·05
7-*Acetamido*-9-*methyl*-	*iodide*	,,	Plates, 189 (decomp.)	$C_{16}H_{17}ON_2I$	—	—	6·65	30·75	—	—	6·85	31·15
	chloride	EtOH–Et_2O	190—191 (decomp.)	$C_{16}H_{17}ON_2Cl$	—	—	8·75	11·05	—	—	8·85	11·2
7-*Amino*-9-*methyl*-,	*chloride hydrochloride*	,,	Hygroscopic)	$C_{14}H_{16}N_2Cl_2$	—	—	9·35	22·8	—	—	9·0	22·85

bromide obtained by metathesis with potassium bromide; it crystallised from water in deep-red needles, m. p. 217° (decomp.) (Found: N, 10·4; Br, 19·75. $C_{31}H_{31}ON_5Br$ requires N, 10·3; Br, 19·6%). The same product was obtained by ferrous hydroxide reduction of 7-amino-9-*p*-nitrobenzoyl-10-methylphenanthridinium chloride. When a warm aqueous solution of the salt was shaken with excess of ethyl chloroformate, 7-carbethoxyamino-9-*p*-aminobenzoyl-10-methylphenanthridinium chloride crystallised, m. p. 198° (decomp.).

7-*Carbethoxyamino*-9-p-*carbethoxyaminobenzylphenanthridine*.—A solution of 7-carbethoxyamino-9-*p*-nitrobenzylphenanthridine (13·3 g.) in alcohol (500 ml.) was treated with stannous chloride (23 g.) and concentrated hydrochloric acid (26·6 ml.) and refluxed for 2 hours. The filtered solution was made strongly alkaline with 5*N*-sodium hydroxide to precipitate 7-*carbethoxyamino*-9-*p*-*aminobenzylphenanthridine* (11 g.), which crystallised from a large volume of benzene in cream-coloured felted needles, m. p. 207—208° (efferv.) (Found: C, 74·7; H, 5·95; N, 11·3. $C_{30}H_{31}O_3N_5$ requires C, 74·35; H, 5·7; N, 11·3%). The crude amine (11 g.) in hot alcohol (350 ml.) was treated with ethyl chloroformate (2·8 ml.) and diethylaniline (5·6 ml.), and refluxed for 30 minutes. The solution was poured into water and the voluminous precipitate was collected and crystallised from aqueous alcohol (charcoal) and then from acetone–light petroleum (b. p. 40—60°), giving the *biscarbethane* as small plates, m. p. 212° (efferv.) (8 g.) (Found: C, 70·15; H, 5·55; N, 9·8. $C_{34}H_{35}O_5N_5$ requires C, 70·4; H, 5·7; N, 9·45%).

7-*Carbethoxyamino*-9-p-*carbethoxyaminobenzoylphenanthridine*.—The foregoing compound (3 g.) in dioxan (65 ml.) and water (3 ml.) was boiled under reflux with selenium dioxide (750 mg.) for 7 hours. The filtered solution was evaporated to dryness, and the residue extracted with boiling acetone. The extract on cooling deposited the *phenanthridine* (2·2 g.), m. p. 242—245° (efferv.), which on recrystallisation from acetone formed small cream-coloured needles, m. p. 247° (efferv.) (Found: C, 68·5; H, 5·7; N, 9·65. $C_{34}H_{33}O_5N_5$ requires C, 68·25; H, 5·05; N, 9·2%). The quaternary salt was obtained by the methyl sulphate–nitrobenzene method. Metathesis in aqueous solution with sodium chloride converted it into 7-*carbethoxyamino*-9-p-*carbethoxyaminobenzoyl*-10-*methylphenanthridinium chloride*, which crystallised from methanol in fine, yellow needles, m. p. 226° (decomp.) (Found: N, 9·45; Cl, 6·95. $C_{37}H_{36}O_5N_5Cl$ requires N, 9·25; Cl, 7·0%). When this salt was hydrolysed with sulphuric acid 7-amino-9-*p*-aminobenzoyl-10-methylphenanthridinium bromide was obtained, identical with that already described.

7-*Carbethoxyamino*-9-p-*acetamidobenzoyl*-10-*methyl*-9 : 10-*dihydrophenanthridine* (IX).—(*a*) A solution of 7-carbethoxyamino-9-*p*-nitrobenzoyl-10-methylphenanthridinium chloride (1 g.) in water (50 ml.) was refluxed gently with iron powder (1 g.) for 1 hour. The insoluble material was extracted with hot methanol, and the evaporated solution allowed to crystallise. The solid (700 mg.) so obtained was recrystallised twice from methanol, giving deep-yellow platelets, m. p. 174—175° (efferv.), shrinking from 170° (Found: C, 71·55; H, 5·3; N, 10·7. $C_{34}H_{33}O_5N_5$ requires C, 71·8; H, 5·8; N, 10·45%).

Acetylation of this compound with acetic anhydride gave a good yield of the *acetyl-dihydro*-compound, which crystallised from methanol in orange-red plates, m. p. 205—210° (efferv.) (Found: C, 70·15; H, 5·6; N, 9·8; Ac, 9·45. $C_{36}H_{35}O_6N_5$ requires C, 70·4; H, 5·7; N, 9·5; Ac (1 per mol), 9·7%). Light absorption in alcohol: maxima, 2580, 2920, 3520 A.; log ε, 4·50, 4·52, 3·94, respectively. (*b*) 7-Carbethoxyamino-9-*p*-aminobenzoyl-10-methylphenanthridinium chloride (500 mg.) was similarly reduced with iron and water, and the crude dihydro-compound (300 mg.) that resulted was acetylated to give the same acetyl derivative (250 mg.). (*c*) 7-Carbethoxyamino-9-*p*-acetamidobenzoyl-10-methylphenanthridinium chloride (350 mg.) on treatment with iron and water gave the identical acetyl-dihydro-compound (250 mg.). (*d*) 7-Carbethoxyamino-9-*p*-aminobenzoyl-10-methylphenanthridinium chloride (500 mg.), suspended in alcohol (25 ml.), was hydrogenated with palladium–charcoal catalyst (250 mg.; 5%) in presence of sodium acetate (100 mg.) until 1 mol. of hydrogen had been absorbed (*ca.* 3 hours). The crude dihydro-compound (250 mg.), isolated by evaporation of the filtered solution to small bulk and precipitation with water, was acetylated to give the acetyl compound (200 mg.) described above.

2 : 7-*Biscarbethoxyamino*-9-*benzylphenanthridine*.—2 : 7-Biscarbethoxyamino-9-benzylphenanthridine (3 g.) in dioxan (60 ml.) and water (1·5 ml.) was refluxed with selenium dioxide (800 mg.) for 7 hours. The solid remaining after evaporation of the filtered solution was crystallised from acetone to give small bright yellow plates of the *benzoyl* compound (2·05 g.), m. p. 241° (efferv.), raised to 244° (efferv.) on recrystallisation from acetone (Found: C, 68·3; H, 4·9; N, 9·05. $C_{31}H_{29}O_5N_5$ requires C, 68·25; H, 5·05; N, 9·2%). Treatment of this base in nitrobenzene solution with excess of methyl sulphate at 150—160° for 5 minutes, followed by conversion of the resulting methosulphate into chloride, gave 2 : 7-*biscarbethoxyamino*-9-*benzoyl*-10-*methylphenanthridinium chloride*, which formed fine orange needles, m. p. 195° (decomp.), from methanol–ethyl acetate (Found: N, 8·05; Cl, 6·65. $C_{33}H_{34}O_5N_5Cl$ requires N, 9·25; Cl, 7·0%). Hydrolysis of this salt (6 g.) with sulphuric acid afforded 2 : 7-*diamino*-9-*benzoyl*-10-*methylphenanthridinium bromide* (X) (4·1 g.), which crystallised from methanol in large deep-purple flat needles, decomposing slowly above 250° (Found: C, 61·55; H, 4·35; N, 10·2; Br, 19·9. $C_{21}H_{18}ON_4Br$ requires C, 61·75; H, 4·45; N, 10·3; Br, 19·6%).

2 : 7-*Biscarbethoxyamino*-9-*benzoyl*-10-*methyl*-9 : 10-*dihydrophenanthridine*.—2 : 7-Biscarbethoxyamino-9-benzoyl-10-methylphenanthridinium chloride (500 mg.) in water (50 ml.) was refluxed gently with iron powder (500 mg.) for 1 hour. The solution was filtered hot, and the residue extracted with boiling alcohol. Water was added to induce crystallisation and the crude product (350 mg.) was crystallised twice from methanol to give the *dihydrophenanthridine* as yellow needles, m. p. 193—195° (efferv.) (Found: C, 68·5; H, 5·85; N, 9·8. $C_{31}H_{31}O_5N_5$ requires C, 68·45; H, 5·75; N, 9·85%). Light absorption in alcohol: Maxima, 2570, 2980, 3520 A.; log ε, 4·53, 4·30, 4·18, respectively.

9-*Phenyl*-10-*methylphenanthridinium Chloride*.—An aqueous suspension of silver chloride and 9-phenyl-10-methylphenanthridinium iodide was refluxed for 20 minutes to give a solution of the *chloride*; this salt crystallised from a small volume of water in colourless prisms, m. p. 211° (decomp.) (Found: N, 4·5; Cl, 11·8. $C_{20}H_{16}NCl$ requires N, 4·6; Cl, 11·6%).

7-*Ethylcarbonato*-9 : 10-*dimethylphenanthridinium bromide* was obtained from 7-ethylcarbonato-9-methylphenanthridine (Copp and Walls, *J.*, 1950, 311) in the usual manner. Its *hemihydrate* crystallised from methanol in buff-coloured prisms which decomposed at 194—195° (bath preheated to 170°) (Found: C, 56·6; H, 5·3. $C_{18}H_{19}O_3NBr,0{\cdot}5H_2O$ requires C, 56·2; H, 5·0%).

7-*Acetamido*-9 : 10-*dimethylphenanthridinium methyl sulphate* was obtained from 7-acetamido-9-methylphenanthridine (*J.*, 1947, 71) by the methyl sulphate–nitrobenzene method, and crystallised from water: small yellow needles, m. p. 275° (decomp.) (Found: N, 7·4; S, 8·35. $C_{18}H_{20}O_6N_2S$ requires N, 7·5; S, 8·5%).

Dihydrophenanthridines.—The most convenient method of preparation was as follows: 9-phenyl-10-methylphenanthridinium chloride (5 g.) was suspended in ethanol (50 ml.), together with sodium acetate (1·1 g.) and Adams's catalyst (200 mg.), and the mixture was shaken under hydrogen at 1—10 atm. pressure. Absorption of hydrogen took place fairly quickly and was complete in about 3 hours when 1 mol. of hydrogen had been absorbed; as reduction progressed a very striking bright-blue fluorescence appeared. On addition of water to the filtered solution the product separated in almost colourless prisms (3·1 g.). The same product resulted on using palladium–charcoal as the catalyst, but the reduction was much slower.

7-*Acetoxy*-9 : 10-*dimethyl*-9 : 10-*dihydrophenanthridine.*—7-Hydroxy-9 : 10-dimethyl-9 : 10-dihydrophenanthridine (1 g.) (Table I) was dissolved in acetic anhydride (4 ml.), and the solution heated under reflux for 15 minutes. After cooling, excess of acetic anhydride was decomposed with water and the insoluble gummy layer crystallised from methanol.

7-*Amino*-9 : 10-*dimethyl*-9 : 10-*dihydrophenanthridine* was obtained by hydrolysis of the acetyl derivative (Table I) with 20% alcoholic hydrochloric acid. On dilution of the reaction mixture with water and neutralisation with ammonia, the amine was precipitated as a gum which could not be induced to crystallise even after distillation in a high vacuum. With acetic anhydride it was reconverted into the acetyl derivative.

Quaternary Salts from Dihydrophenanthridines.—The compounds of Table II were prepared by the following method. 9-Phenyl-10-methyl-9 : 10-dihydrophenanthridine (4·6 g.) was suspended in a mixture of methanol (46 ml.) and methyl iodide (9·2 ml.), and the mixture refluxed for 12 hours. After cooling, the crystalline methiodide (5·6 g.) was collected and recrystallised from hot water.

7-*Hydroxy*-9 : 10 : 10-*trimethyl*-9 : 10-*dihydrophenanthridinium Iodide.*—A solution of 7-acetoxy-9 : 10 : 10-trimethyl-9 : 10-dihydrophenanthridinium iodide (1 g.) in dilute hydrochloric acid (10 ml.) was heated on the steam-bath for 45 minutes. The cooled solution (charcoal) was evaporated in a vacuum; the residue was redissolved in a little water and excess potassium iodide added, and the gum that was precipitated crystallised from water.

7-*Amino*-9 : 10 : 10-*trimethyl*-9 : 10-*dihydrophenanthridinium Chloride Hydrochloride.*—7-Acetamido-9 : 10 : 10-trimethyl-9 : 10-dihydrophenanthridinium chloride (1 g.) was refluxed with 2*N*-hydrochloric acid (5 ml.) for 2 hours. The solution was then evaporated to dryness under reduced pressure, and the residual gum dissolved in dry alcohol. After addition of ether colourless prisms of the hygroscopic hydrochloride separated.

The authors thank Mr. L. G. Goodwin and his colleagues of the Wellcome Laboratories of Tropical Medicine for examination of the trypanocidal properties of many of these compounds, Messrs. A. R. Brown, W. E. King, and R. G. W. Spickett for valuable assistance, Mr. A. Bennett for microanalyses, and Dr. T. S. G. Jones for the light-absorption measurements.

CHEMICAL DIVISION, WELLCOME RESEARCH LABORATORIES,
BECKENHAM, KENT.

[*Received, May 4th*, 1950.]

---

519. *Chemical Actions of Ionising Radiations on Aqueous Solutions. Part V. Hydroxylation of Nitrobenzene by Free Radicals produced by X-Rays.*

By (MISS) H. LOEBL, GABRIEL STEIN, and JOSEPH WEISS.

Following the quantitative investigation of the hydroxylation of nitrobenzene by free hydroxyl radicals produced by the hydrogen peroxide–ferrous salt reagent (*J.*, 1949, 2074), it is now shown that the action of *X*-rays on dilute aqueous solutions of nitrobenzene leads to the same products. The ratio of the *o*-, *m*-, and *p*-isomers is essentially the same as in the previous case, thus confirming again the assumption of free-radical formation by ionising radiations. The use of this method enables one to employ more refined analytical techniques and to study the effect of pH on the relative ratio of the various products. It is shown that the position occupied by the nitro-group is also attacked, resulting in a denitration with the formation of nitric acid. The quantitative results are in agreement with a reaction mechanism involving two distinct steps (*J.*, 1949, 3245).

IN a previous paper (*J.*, 1949, 2074) we discussed the action of Fenton's hydrogen peroxide–ferrous salt reagent on dilute aqueous solutions of nitrobenzene. This reagent is well known to yield free hydroxyl radicals (Haber and Weiss, *Proc. Roy. Soc.*, *A*, 1934, **147**, 332) and our main

interest was in the quantitative relationship between the three isomeric nitrophenols which can be formed in the attack of these radicals on nitrobenzene. However, this reagent does not lend itself readily to quantitative work, especially when the resulting products are phenolic. The decomposition of hydrogen peroxide makes reproducibility difficult, and the ferric salt formed in the reaction interacts with the phenolic product forming complex products, and in certain cases it is capable of oxidising them further to yield quinonoid products. Moreover, the pH of the solution must be kept within rather narrow limits to prevent the precipitation of the iron salts.

Using Fenton's reagent, we have shown that all three isomers are formed, and the rather crude estimate possible gave their proportions approximately as *o*- 25—30%, *p*- 50—55%, *m*- 20—25% of the total monohydroxy-nitrobenzenes produced. In addition we have demonstrated the formation of 3 : 3'-dinitrodiphenyl. This indicated the intermediate formation of free nitrophenyl radicals in the reaction. Subsequently, Merz and Waters (*J.*, 1949, 2427) also isolated *o*-nitrophenol in a similar reaction, but not the *m*- or the *p*-isomer.

Recently, we have shown (Stein and Weiss, *Nature*, 1948, **161**, 650; *J.*, 1949, 3245) that the action of ionising radiations on dilute aqueous solutions results in formation of free radicals according to :

$$H_2O \longrightarrow\!\!\!\!\!\sim\!\!\!\!\!\sim\!\!\!\!\!\sim

The analytical procedure employed involved the separation of the *o*-nitrophenol (and the unchanged nitrobenzene) from the other (non-volatile) products of the reaction by steam-distillation *in vacuo* at a temperature of about 40°. The *o*-nitrophenol in the distillate was determined colorimetrically. The residue from the steam-distillation was further separated into neutral and phenolic fractions, and the resulting mixture of *m*- and *p*-nitrophenol analysed by infra-red absorption spectroscopy.

The yield of *o*-nitrophenol (at pH ~6) is shown in Fig. 1 and is seen to be linear with the dose as long as sufficient oxygen is present to react according to equation (2). Fig. 1 should be compared with the similar figures given for benzene (*loc. cit.*).

The results obtained for the ratio of the three isomeric nitrophenols at different pH values are given in Table I. Each of the results is the mean of at least three independent experiments

TABLE I.

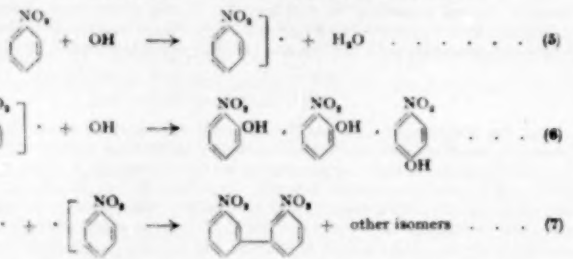
Yield of nitrophenols at different pH values in 200 ml. of saturated solution of nitrobenzene in water. (Dose : $3{\cdot}5 \times 10^4$ E.U., given in the presence of air.)

		Percentage of total,		
pH.	Total nitrophenols (mg.).	*o*.	*m*.	*p*.
2	1·23	34·5	31	34·5
6	1·07	35·5	29	35·5
12	0·90	27·5	27	45·5

(see Experimental). The values for *o*-nitrophenol were within $\pm 5\%$; those for the *m*- and the *p*-isomer, which were obtained by infra-red analysis, were within $\pm 10\%$ of the mean values given in Table I. These results show once again that from nitrobenzene all three possible isomers are formed, unlike the case of phenol, where only the *o*- and the *p*-isomer are apparently formed (Stein, Thesis, *loc. cit.*; Stein and Weiss, in preparation). The relative ratios depend on the pH of the solution, as does the total amount of nitrophenols formed. The ratio obtained when using Fenton's reagent agrees well with the more accurate determinations now recorded. One can now claim with some confidence that the use of ionising radiations as a means of investigating the reactions of the free OH (and HO_2) radicals is justified.

The monohydroxynitrobenzenes thus estimated comprise, however, only 40—50% of the total reaction products. The remainder can be separated into different parts, and it was thus shown that the amount of the neutral fraction, consisting mainly of dinitrodiphenyl, was, in experiments carried out at pH ~6, only slightly less by weight than that of the total nitrophenols; hence, both together account for about 80—85% of the total reaction products. The residue had a phenolic character and consisted largely of phenol, and to a less extent of nitrophenols (probably dinitrodiphenols and dihydroxynitrobenzenes, giving a red colour in alkaline solution). The mode of formation of the phenol will be discussed below.

The results once again support the hypothesis of a two-step attack according to :



Reaction (7), affording dinitrodiphenyl, which has been isolated, presumes the occurrence of reaction (5), since in no other way can even the qualitative results (Loebl, Stein, and Weiss, *loc. cit.*; Merz and Waters, *loc. cit.*) be explained. In addition, it has been shown in the similar case of benzene (*loc. cit.*) that the quantitative relationships obtained are not compatible with any other mechanism. The ratio of the isomers found here, together with our preliminary results on the hydroxylation of phenol, showing the absence of the *m*-isomer, resorcinol, indicate

the operation of a directive effect in these free-radical substitutions. The detailed discussion will be postponed till the completion of our work on some other monosubstituted benzene derivatives.

FIG. 1.

Dependence of the yield of o-nitrophenol on the X-ray dose (air-saturated solutions at pH ~ 6).

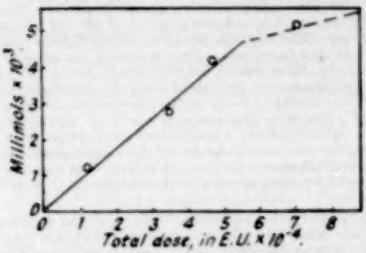
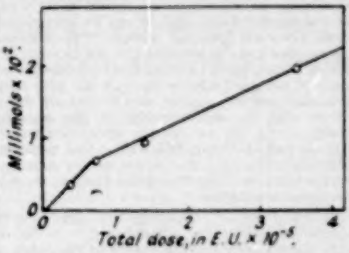
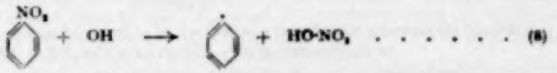


FIG. 2.

Dependence of the yield of nitrate ion on the X-ray dose (air-saturated solutions at pH ~ 6).



The substitution reactions discussed above accounted for the attack at the 2-, 3-, 4-, 5-, and 6-positions of the nitrobenzene ring. There was, however, reason to suppose that position 1 might also be susceptible to attack by the radicals, for it has been shown (Fichter and Bonhôte, *Helv. Chim. Acta*, 1920, **3**, 395) that in electrolytic oxidations, which presumably involve free hydroxyl radicals as intermediates, the nitro-group attached to an aromatic ring can be removed. We have therefore investigated the possibility of the formation of nitrate in our reaction, *e.g.*, according to :

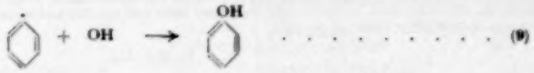


(8)

which assumes that the position occupied by the nitro-group is in some way analogous to the other positions. In fact we have been able to demonstrate the formation of nitrate in the irradiated solution. Fig. 2 shows the dependence of the yield of nitrate ion on the dose at pH ~6. The decline of the yield per unit dose after exhaustion of the dissolved oxygen points to the formation of nitrate ion being in fact due to hydroxyl radicals, and not to hydrogen atoms. We have not found any nitrite in our experiments.

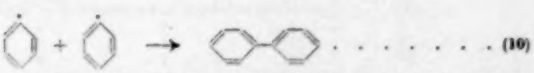
Experiments on the influence of pH on the formation of the nitrate ion have yielded identical amounts at pH values of approximately 2, 6, and 12. Since, however, the determination of nitrate in the very small amounts present was open to an error of not less than ±10%, all we can say is that the amount formed is apparently not appreciably influenced by the pH, and probably less so than the ratio of hydroxylated isomers. The amount of nitrate ion formed was about equivalent to one of the phenolic isomers formed at pH 6.

Reaction (8) should result in the formation of free phenyl radicals, which may further react according to :



(9)

or



(10)

as well as with the formation of products containing the nitro-group in one ring only. Reaction (9) will then be the source of the phenol which we have found.

EXPERIMENTAL.

Irradiation Arrangements.—These were identical with those described in Parts I and II (*loc. cit.*). A Victor Maximar set was used at 200 kv. and 15 ma., without filtration. The dose was determined by the method of Day and Stein (*loc. cit.*), and found to be 2350 E.U./min.

Nitrobenzene Solution.—Redistilled nitrobenzene was used to saturate distilled water. Further purification of the water does not influence our results. 200-Ml. portions were irradiated at a time. All irradiations were carried out in the presence of air. Acid pH values were maintained with sulphuric acid, alkaline values by sodium hydroxide.

Separation of the Reaction Mixture.—Several batches of irradiated solutions were united and acidified, and the excess of nitrobenzene, with all the *o*-nitrophenol, steam-distilled in a vacuum at approx. 40° into dilute alkali. Experiments on synthetic mixtures of the three isomeric nitrophenols showed that it is possible to determine these separately as follows. The *o*-nitrophenol as above, the yellow colour in the alkaline solution being measured directly on a Spekker colorimeter by use of Ilford filter No. 602. In the residue the *p*-nitrophenol can be determined similarly in a buffered solution at pH 7·0, where the *m*-isomer does not give any colour. The *m*-isomer can then be determined by using Folin's reagent, this being the only isomer which reacts with it. It has been impossible, however, to employ this procedure, which gave very satisfactory results on synthetic mixtures, since in irradiated solutions the presence of the dinitrodiphenols and the dihydroxynitrobenzenes interfered with the determination of the *p*-isomer, and the phenol, which does not distil over quantitatively under the conditions described, interfered with the determination of the *m*-isomer. However the *o*-isomer could be determined as described above, by exhaustive steam-distillation, which affords quantitative separation from the isomers (Arnall, *J.*, 1924, **125**, 811). Our experience on the determination of the *o*-nitrophenol in the distillate by measuring the yellow colour developed in alkaline solution has shown that reproducible results are obtained, and the calibration curve, obtained by using synthetic material (recryst., m. p. 44°), gave a linear dependence.

Detection of phenol. The distillate containing the *o*-nitrophenol gives the Folin test characteristic of phenol but not given by *o*-nitrophenol. On the other hand, the presence of phenol does not interfere with the colorimetric determination of the *o*-nitrophenol as described: only part of the phenol distils over under these conditions. The phenol in the residue does not interfere with the determination of *m*- and *p*-nitrophenols by the infra-red method.

The residue after distillation was extracted exhaustively with ether. The ethereal extract was either evaporated to dryness and weighed, giving the sum of all products except the *o*-nitrophenol, or extracted with alkali and then evaporated, giving the neutral fraction. The original ethereal extract, or in the second case the ethereal extract of the acidified phenol fraction, was then evaporated and submitted to infra-red analysis. Table II shows in greater detail some of the results obtained and the reproducibility of our experiments.

TABLE II.

Yields of the isomeric nitrophenols in 200 ml. of a saturated aqueous solution of nitrobenzene, in the presence of air. (Dose: approx. $3{\cdot}5 \times 10^4$ E.U.)

	Yield, mg.			% of isomers.				Yield, mg.			% of isomers.		
pH.	*o*-.	*m*-.	*p*-.	*o*-.	*m*-.	*p*-.	pH.	*o*-.	*m*-.	*p*-.	*o*-.	*m*-.	*p*-.
2	0·41	0·36	0·47	33·5	29	37·5	6	0·35	0·28	0·36	35·5	28	36·5
2	0·43	0·40	0·38	35	33·5	31·5	6	0·40	0·34	0·40	35	30	35
2	0·42	0·35	0·42	35·5	29	35·5	12	0·24	0·21	0·44	28	23	49
2	0·42	0·43	0·42	33	34	33	12	0·24	0·28	0·39	27	30	43
6	0·38	0·31	0·38	35·5	29	35·5	12	0·27	0·26	0·38	28	29	43

Determination of Nitrate.—The presence of nitrate ion was proved by means of brucine, diphenylbenzidine, and pyrogallol (see Snell, "Colorimetric Methods of Analysis," Vol. I., pp. 635, 638, 641), and we used Haase's brucine reaction (see Snell, *loc. cit.*) for the quantitative determination of nitrate. Calibration curves were obtained by using "AnalaR" potassium nitrate; blank tests were carried out using un-irradiated solutions and synthetic mixtures containing the other products of the reaction. Even this method, however, does not give very consistent results. It involves the destruction of all nitrophenols in the sample with concentrated sulphuric acid and potassium permanganate before addition of the reagent, and we found that, although different experiments carried out on the same day with the same batch of reagents agreed very well among themselves, yet they did not agree with experiments carried out on other days. Table III shows some results obtained by this colorimetric method, those in each vertical column being obtained on the same day. It is clear that the yield of nitrate is but little affected by pH.

TABLE III.

pH.	Extinction (arbitrary units measured on Spekker photometer).			
2	14	9	8	10
6	14	11	8	9
12	13	9	8	8

Tests for Nitrite.—To ascertain whether nitrite ion is formed in the reaction, the Griess test (cf. Feigl, "Qualitative Analysis by Spot Tests," 1939, p. 215) and that due to Parker (*Analyst*, 1949, **74**, 112), using naphthylamine hydrochloride in alcohol, have been employed. These were very sensitive with synthetic mixtures containing potassium nitrite, and gave negative results on irradiated solutions.

Infra-red analyses were very kindly carried out by the Physical Chemistry Division, Imperial Chemical Industries Limited, Billingham. Nitromethane was used as solvent, calibration curves being taken with authentic samples of the single components and their mixtures.

We thank Dr. R. Holroyd and Dr. B. W. Bradford, of Imperial Chemical Industries Limited, Billingham, for permission to have the infra-red analyses made in their department, and Mrs. M. Broomfield for help in carrying them out. We also thank Dr. F. T. Farmer and Mr. M. J. Day, of the Radium Department, Royal Victoria Infirmary, for their assistance regarding the irradiations. Our thanks are offered to the North of England Council of the B.E.C.C. for financial support.

KING'S COLLEGE, UNIVERSITY OF DURHAM, NEWCASTLE-ON-TYNE. [*Received, May 17th*, 1950.]

---

520. *Chemical Actions of Ionising Radiations in Solution. Part VI. Radiation Chemistry of Sterols. The Action of X-Rays on Cholesterol and 3β-Hydroxypregn-5-en-20-one.*

By MAX KELLER and JOSEPH WEISS.

In continuation of previous work on the chemical action of ionising radiations and the formation of free radicals and atoms in these processes (Parts I—IV, *J.*, 1949, 3241—3263; Part V, *J.*, 1950, 2704) we have investigated the action of *X*-rays on cholesterol and 3β-hydroxypregn-5-en-20-one in aqueous systems. From the irradiated solutions we were able to isolate, and to characterise by unambiguous methods, from the former cholestane-3β : 5α : 6β-triol and 3β-hydroxycholest-5-ene-7-one, and from the latter 3β : 5 : 6β-trihydroxy*allo*pregnane-20-one. These substances are formed in relatively good yields and account for 80—90% of the starting materials. The outline of a mechanism of the formation of these compounds is given on the basis of the general theory put forward in 1944 (Weiss, *Nature*, **153**, 748), and some possible biological implications of these findings are briefly discussed.

STEROID compounds are widely distributed in the human and animal body and it is well known that steroid hormones are among the controlling factors in metabolism. In recent years it has also become increasingly more probable that sterol metabolism has a bearing on the incidence of cancer; it is well known that irradiation by *X*-rays can both lead to cancer and, conversely, arrest the development of malignant tissue already present in the organism. For these reasons and also from a general chemical point of view, it seemed of interest to study the chemical changes produced by ionising radiations on naturally occurring sterols and related compounds, particularly as no relevant information appears to exist in the literature.

In the present paper we report a study of the action of *X*-rays on cholesterol (I) and 3β-hydroxypregn-5-en-20-one (IX) in aqueous systems.

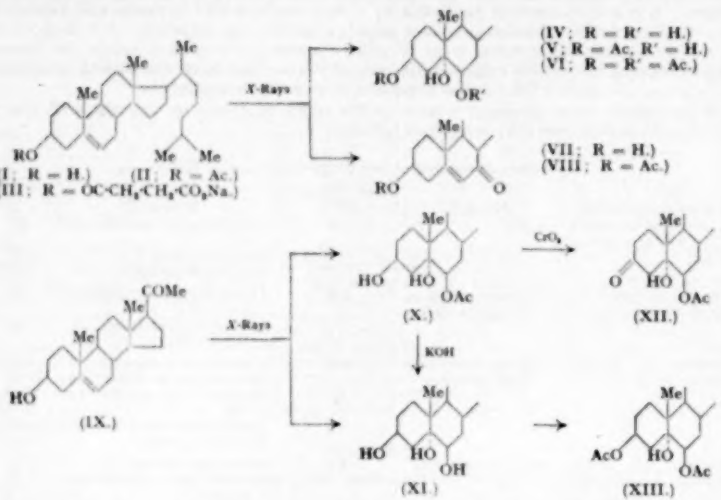
Irradiation of cholesterol and pregn-5-enolone by X-*rays.*

Substance irradiated.	Solvent.	Dose (approx.), 10^6 r.	Products.	Yield, %	
Na cholesteryl succinate (III), 0·25% solution (in air)	Water	1·8	Cholestane-3β : 5α : 6β-triol (IV)	19	84
			Unidentified oil	~15	
			Starting material	50	
Cholesteryl acetate (II), 0·17% solution (in air)	Aqueous acetic acid (10% of water)	1·8	3β : 6β-Diacetoxycholestan-5-α-ol (VI)	32	80
			3β-Acetoxycholestane-5α : 6β-diol (V)	48	
Cholesterol (I), 0·16% solution (in air)	Aqueous acetic acid (10% of water)	3·6	Cholesteryl acetate (II)	4·5	80
			3β-Cholest-5-en-7-one (VII)	17·5	
			Cholestane-3β : 5α : 6β-triol (IV)	27·5	
			Unidentified oil	~5	
			Starting material	25	
Cholesterol (I), 0·5% solution (in a vacuum)	Glacial acetic acid	2·1	Cholesteryl acetate (II)	7	94
			3β : 6β-Diacetoxycholestan-5α-ol (VI)	4	
			3β-Hydroxycholest-5-en-7-one (VII)	7	
			Unidentified oil	~4	
			Starting material	72	
3β-Hydroxypregn-5-en-20-one (IX), 0·3% solution (in air)	Aqueous acetic acid (10% of water)	2·7	6β-Acetoxy-3β : 5α-dihydroxy*allo*pregnan-20-one (X)	18	74
			3β : 5α : 6β-Trihydroxy*allo*pregnan-20-one (XI)	25	
			Starting material	31	

Cholesterol is present in the human blood-stream and in living tissue and is known to be a precursor in the biosynthesis of the sex hormones and of the hormones of the adrenal cortex (cf. Pincus and Thimann, "The Hormones," Vol. I, New York, 1948). Pregn-5-enolone, which is chemically similar to cholesterol (it differs in the side chain), is closely related to the sex hormones. In view of the absolute lack of knowledge regarding these *X*-radiation reactions our first aim was to establish with certainty the nature of the chemical compounds formed. Since purely physical methods did not appear sufficiently conclusive we have isolated the reaction products and characterised them by unambiguous methods. Therefore, as in our previous work (*loc. cit.*) we had to employ fairly large doses (of the order of 10^6 r.). For separating the reaction products we used elution chromatography, which gave recoveries so good that we were always able to account for 80—90% of the starting material (see Table). Our aim was to work in aqueous systems as these most closely correspond to biological conditions. Cholesterol being itself insoluble in water we first irradiated aqueous solutions of sodium cholesteryl succinate. We found, however, that similar products were obtained in aqueous acetic acid and have used the latter solvent extensively for our sterol work.

In order to study the role of the acetic acid itself we have also carried out irradiations in anhydrous acetic acid. Table I summarises the results obtained under different conditions. *X*-Ray doses were always of the order of 10^6 r. with an average dose rate of approx. 3000 r. The products were identified by their melting points, mixed melting points, analyses, and optical rotations. From the hydroxy-compounds the acetyl derivatives were also prepared, and from 6β-acetoxy-3β : 5α-dihydroxy*allo*pregnan-20-one (X) the corresponding diketone (XII).

The annexed schemes show the products obtained. In general 0·5—1 g. of starting material was used, and in nearly all cases ample amounts were obtained for the identification. We also obtained a few substances as unidentified oils, and two crystalline substances in insufficient amount for complete analysis.



Among the substances which have been isolated cholestane-3β : 5α : 6β-triol is of particular interest as it has been isolated recently from arteriosclerotic aortas by Hardegger, Ruzicka, and Tagmann (*Helv. Chim. Acta*, 1943, **26**, 2205), from pig's testes by Ruzicka and Prelog (*ibid.*, p. 975), and from beef liver by Haslewood (*Biochem. J.*, 1941, **35**, 708). The 7-ketone (VII) has been isolated from bull's testes by Steinmann (*Helv. Chim. Acta*, 1943, **26**, 2222) and from pig's testes by Prelog, Tagmann, Liebermann, and Ruzicka (*ibid.*, 1947, **30**, 1080).

Although relatively large doses of *X*-rays had to be employed in this work the excellent yields and the relatively simple changes involved make it highly probable that essentially the

same substances would be also formed with the small doses which are used under biological conditions.

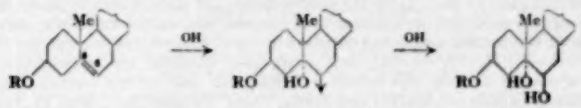
Discussion.—Until relatively recently the chemical action of ionising radiations was considered to involve intervention of special excited molecules or ionic species not encountered in "ordinary" chemistry. The general theory put forward in 1944 (Weiss, *Nature*, **153**, 748) in a sense reduces radiation chemistry to the chemistry of free radicals, about which we already possess information from independent sources. In radiation chemistry the formation of free radicals is based on the assumption that the primarily-formed ionic species are unstable (especially in the presence of a polar solvent) and decompose rapidly into radicals and atoms and more stable ions. In the case of water the active radicals were shown to be hydroxyl radicals and hydrogen atoms (Parts II—V, *loc. cit.*) which are presumed to be formed from the primary ions :

$$H_2O^+ \rightleftharpoons OH + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$H_2O^- \rightleftharpoons H + OH^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

For aqueous solutions this accounts for all the experimental facts, and the formation of hydroxyl radicals and hydrogen atoms has been amply confirmed (*loc. cit.*). On the basis of the results already obtained it seemed hopeful to study the action of ionising radiations on more complicated molecules of biological importance [cf. Part IV (amino acids) and work on nucleic acids (Scholes, Stein, and Weiss, *Nature*, 1949, **164**, 709].

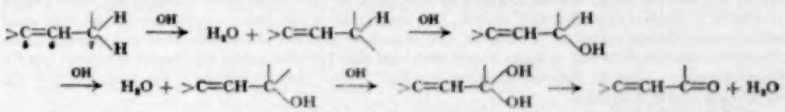
The formation of the triol (IV) is explained by the action of hydroxyl radicals, followed by further addition of hydroxyl radicals to the double bond :



with the intermediate formation of a free radical either from $C_{(5)}$ or from $C_{(6)}$ according to which end of the double bond is attacked first.

A similar process presumably takes place in the aqueous acetic acid solutions of cholesterol (I) or of 3β-hydroxypregn-5-en-20-one (IX), the corresponding triols (IV) and (XI) having been isolated from the irradiated solutions.

The starting materials differ only in their side chain and it is reasonable to expect that this, being rather remote from the point of attack, does not appreciably influence the reactivity of the double bond. In the case of cholesterol the 7-ketone has also been isolated. This can be explained by an attack of the 7-position by hydroxyl radicals, *e.g.*, in the following stages :



The fact that the formation of the ketone requires (by almost any reasonable mechanism) four steps makes its production perhaps less probable, although 4-step processes are by no means uncommon as a result of *X*-ray action (cf. the formation of catechol or quinol from benzene, Part II, *loc. cit.*).

Irradiation in aqueous acetic acid often leads to acetylated compounds. Irradiation of cholesterol in anhydrous acetic acid gave the diacetate of the triol (VI) and the 7-ketone (VII). These results suggest the following tentative picture for the action of *X*-rays on acetic acid. The primarily-formed ions are presumably $[CH_3{\cdot}CO_2H]^+$ and $[CH_3{\cdot}CO_2H]^-$, which can decompose in the following ways :

$$[CH_3{\cdot}CO_2H]^+ \longrightarrow CH_3{\cdot}CO^+ + OH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4a)$$

$$[CH_3{\cdot}CO_2H]^+ \longrightarrow CH_3{\cdot}CO_2 + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4b)$$

$$[CH_3{\cdot}CO_2H]^- \longrightarrow CH_3{\cdot}CO + OH^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5a)$$

$$[CH_3{\cdot}CO_2H]^- \longrightarrow CH_3CO_2^- + H \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5b)$$

Thus in irradiated acetic acid the same radicals (OH and H) could be formed as in water. The presence of hydroxyl radicals is supported by the facts that irradiation of cholesterol in anhydrous

acetic acid also yields 3β : 6β-diacetoxycholestan-5α-ol (VI) (which contains a hydroxyl group) and the 7-ketone (VII) (which is presumably also formed by the action of hydroxyl radicals (see above). On the other hand, in this experiment, carried out in the absence of atmospheric oxygen, no molecular hydrogen could be detected. This suggests that reaction (5*a*) takes place in preference to reaction (5*b*) or else, what seems less likely, that any hydrogen atoms formed are taken up by some of the other radicals, *e.g.*, $H + OH \longrightarrow H_2O$ or $H + CH_3{\cdot}CO_2 \longrightarrow CH_3{\cdot}CO_2H$, or by some of the other acceptors present. The presence of the acetylated products can be variously accounted for. A possible explanation is that the hydroxy-compounds are first formed by the action of hydroxyl radicals and then acetylated. According to recent work by Burton and Praill (*J.*, 1950, 1203) the acetylium ion, $CH_3{\cdot}CO^+$, which is formed here according to reaction (4*a*) is a very powerful acetylating agent, reacting with hydroxyl groups according to

$$R{\cdot}OH + CH_3{\cdot}CO^+ \longrightarrow RO{\cdot}CO{\cdot}CH_3 + H^+$$

In the presence of water it will presumably react preferentially therewith. However, there is also the possibility of a 2-step free-radical acetylation, *viz.* :

$$R{\cdot}OH + OH \longrightarrow RO{\cdot} + H_2O$$

or

$$R{\cdot}OH + CH_3{\cdot}CO_2 \longrightarrow RO{\cdot} + CH_3{\cdot}CO_2H$$

followed by

$$RO{\cdot} + CH_2{\cdot}CO \longrightarrow RO{\cdot}CO{\cdot}CH_3$$

and the acetyl group on $C_{(6)}$ could be formed also simply by the direct addition of $CH_3{\cdot}CO_2$ [formed in reaction (4*b*)] to the $C_{(6)}$ of the double bond. It should also be borne in mind that some of the radicals produced in the reactions (4) and (5) could form acetic anhydride. If $CH_3{\cdot}CO_2$ radicals are formed according to reaction (4*b*) or from the solvent by the reaction $CH_3{\cdot}CO_2H + OH \longrightarrow CH_2{\cdot}CO_2{\cdot} + H_2O$, one must also consider the appearance of methyl radicals and of carbon dioxide, the former of which can lead to the formation of methane, ethane, and other products (cf. Walker and Weiss, *Trans. Faraday Soc.*, 1935, **31**, 1011; Clusius and Schanzer, *Ber.*, 1942, **75**, 1795; *Z. physikal. Chem.*, 1943, **192**, *A*, 273).

We have also considered the possibility of the intermediate formation of epoxides which could be transformed into the triols or their acetylated products. However, no evidence could be obtained of the presence of an epoxide among the products of the irradiation of either cholesterol or the pregnenolone. Further, it is known that hydrolysis or acetolysis of the epoxides requires prolonged heating with acetic acid (cf. Lettré and Hagedorn, *Z. physiol. Chem.*, 1936, **242**, 210; Davis and Petrow, *J.*, 1950, 1185).

The results available do not permit a full quantitative discussion, and only certain suggestions can be put forward at present. However, one may conclude that there is a great tendency for hydroxyl radicals to attack an isolated double bond in the sterol ring, yielding dihydroxylated products if these are sufficiently stable. If the latter is not the case, fission of the ring may occur (unpublished results). However, the attack by hydroxyl radicals does not appear to be altogether confined to the double bonds and can also involve labile hydrogen atoms in partly unsaturated or even in saturated sterol systems. The former is shown, for instance, by the formation of the 7-ketone.

Perhaps one of the most striking features of the work reported in this paper is that in the action of *X*-rays only one or two products are formed predominantly and in relatively high yields. This is, at first sight, surprising but it is most fortunate from an experimental point of view. One must conclude that the 7-ketone and particularly the triols from cholesterol and pregnenolone are rather stable towards further attack. The formation of triols constitutes a relatively simple change of the molecule and probably occurs already with very small doses. It may well be that it is connected with steroid metabolism, particularly as the triol from cholesterol has been isolated from various tissues (*loc. cit.*).

Experimental.

Irradiations were carried out as described in Parts I, II, and IV of this series (*loc. cit.*).

Action of X-Rays on Sodium Cholesteryl Succinate in Aqueous Solution.—The sodium salt (III) (1·5 g.) in distilled water (600 ml.) was irradiated for 10 hours at 30—35°. The solution was then acidified with hydrochloric acid and extracted with ether, the ethereal extract washed till neutral and dried (Na_2SO_4), and the ether distilled off in a vacuum. The residue was heated under reflux with potassium carbonate (3·5 g.) in methanol (50 ml.) and water (10 ml.) for 1½ hours. The methanol was removed in a vacuum and the residue extracted with ether, the ethereal extract washed and dried (Na_2SO_4), the ether distilled off, and the crude product (about 1 g.) chromatographed through alumina (30 g.). Elution with ben-

sene and benzene–ether (10 : 1), followed by crystallisation from methanol, gave cholesterol (500 mg.), m. p. 145—147°, not depressed on admixture with a pure specimen. Elution with ether gave an oil (150 mg.) which could not be crystallised. Elution with chloroform–methanol (10 : 1) gave, after repeated crystallisation from methanol and ethyl acetate, cholestane-3β : 5α : 6β-triol (IV) (200 mg.), m. p. 231—235°, not depressed on admixture with an authentic specimen [prepared by hydrolysis of the diacetate (VI) which was kindly supplied by Dr. M. Davis (see Davis and Fetrow, *J.*, 1949, 2536)] (Found : C, 76·5; H, 11·0. Calc. for $C_{27}H_{48}O_3$: C, 77·1; H, 11·5%). Acetylation gave the 3β : 6β-diacetate, m. p. 168—169° (from methanol) (not depressed on admixture with authentic specimen obtained from Dr. Davis), $[\alpha]_D^{25}$ −46·12° ± 2° (*c*, 4·098 in chloroform) (Plattner and Lang, *Helv. Chim. Acta*, 1944, **27**, 1872, give $[\alpha]_D$ −44·9°, −47·5° in chloroform).

Action of X-*Rays on Cholesterol in Aqueous Acetic Acid.*—Cholesterol (1 g. ; purified by chromatography) in aqueous acetic acid (600 ml. ; containing 10% of water) was irradiated for 20 hours at 30—35°. The solvent was removed at reduced pressure at 35°, the residue extracted with ether, and the extract washed until neutral. After removal of the ether the crude product (0·95 g.) was chromatographed through alumina (30 g.). Elution with light petroleum–benzene (5 : 1) followed by crystallisation from methanol gave cholesteryl acetate (50 mg.), m. p. 113—115°, not depressed on admixture with an authentic specimen. Elution with benzene and with benzene–ether (5 : 2) gave unchanged cholesterol (250 mg.), m. p. 147—148°. Elution with benzene–ether (1 : 1) and crystallisation from methanol gave 3β-hydroxycholest-5-en-7-one (VII) (180 mg.) (Found : C, 80·5; H, 10·9. Calc. for $C_{27}H_{44}O_2$: C, 80·9; H, 11·1%), m. p. 165—167°, not depressed on admixture with an authentic specimen (prepared according to Windaus, Lettré, and Schenck, *Annalen*, 1935, **520**, 98), $[\alpha]_D^{25}$ −109° ± 2° (*c*, 2·169 in chloroform) (Bergström and Wintersteiner, *J. Biol. Chem.*, 1941, **141**, 602, give $[\alpha]_D^{25}$ −104° in chloroform ; Prelog, Liebermann, and Ruzicka, *Helv. Chim. Acta*, 1947, **30**, 1080, give $[\alpha]_D^{25}$ −111° in chloroform). Acetylation of (VII) in pyridine with acetic anhydride gave the 3β-acetate, m. p. 156—158° (from methanol), not depressed on admixture with an authentic specimen. Elution with ether resulted in an oil (50 mg.). This oil, by acetylation and crystallisation from methanol, gave 30 mg. of an unidentified substance (needles) having m. p. 105—107° (Found : C, 82·9; H, 10·9%). Elution with chloroform and chloroform–methanol (20 : 1) and crystallisation from methanol gave cholestane-3β : 5α : 6β-triol (IV) (300 mg.), m. p. 228—235°, not depressed on admixture with an authentic specimen (hydrolysis product of Dr. Davis's preparation). Acetylation of (IV) gave the diacetate (VI), m. p. 165—167° (from methanol) [not depressed on admixture with an authentic specimen (Dr. Davis)] (Found : C, 73·6; H, 10·3. Calc. for $C_{31}H_{52}O_4$: C, 73·8; H, 10·4%), $[\alpha]_D^{25}$ −49·1° ± 2° (*c*, 2·831 in chloroform).

Action of X-*Rays on Cholesteryl Acetate.*—Cholesteryl acetate (1·1 g. ; purified by chromatography) in aqueous acetic acid (600 ml. ; 10% of water) was irradiated for 10 hours at 30—35°. The irradiated solution was treated as in the case of cholesterol, and the crude product (1·5 g.) was subjected to chromatography. Elution with light petroleum–benzene (1 : 1) and benzene, followed by crystallisation from methanol, gave 3β : 6β-diacetoxycholestan-5α-ol (VI) (380 mg.), m. p. 168—169° [not depressed on admixture with an authentic specimen (Dr. Davis)] (Found : C, 73·6; H, 10·2%). Elution with benzene–ether (10 : 1, later 4 : 1), followed by crystallisation from methanol, gave 3β-acetoxycholestane-5α : 6β-diol (V) (523 mg.), m. p. 207—209° (not depressed on admixture with an authentic specimen) (Found : C, 75·3; H, 10·9. Calc. for $C_{29}H_{50}O_4$: C, 75·3; H, 10·9%). Acetylation gave the diacetate (VI), m. p. 168—169° (from methanol) (not depressed on admixture with authentic specimen) (Found : C, 73·4; H, 10·1%).

Action of X-*Rays on Cholesterol in Anhydrous Acetic Acid.*—A solution of cholesterol (500 mg.) in glacial acetic acid (100 ml.) was irradiated in absence of air for 12 hours at 30—35°. The crude product (503 mg.), isolated as above, was chromatographed through alumina (15 g.). Elution with light petroleum–benzene (2 : 1, later 3 : 2) followed by crystallisation from methanol gave cholesteryl acetate (40 mg.), m. p. 113—115°. Elution with benzene–ether (2 : 1, later 1 : 2) followed by crystallisation from ethanol gave unchanged starting material (361 mg.), m. p. 146—148°. Elution with benzene–ether (1 : 4) followed by crystallisation from methanol gave the diacetate (VI) (26 mg.), m. p. 165—166°, not depressed on admixture with an authentic specimen (from Dr. Davis). Elution with ether–chloroform (4 : 1, later 3 : 2) followed by crystallisation from ether–pentane gave 3β-hydroxycholest-5-en-7-one (VII) (30 mg.), m. p. 166—168°, not depressed on admixture with an authentic specimen. Elution with ether–chloroform (2 : 3) gave unidentified small needles (2 mg.), m. p. 139—141° (from methanol). Elution with chloroform resulted in an oil (18 mg.) which did not crystallise.

Action of X-*Rays on 3β-Hydroxypregn-5-en-20-one in Aqueous Acetic Acid.*—A saturated solution of the substance (IX) (2 g.) in aqueous acetic acid (600 ml., containing 10% of water) was exposed to *X*-rays for 15 hours at 30—35°. The acetic acid was removed at reduced pressure at 35—40° and the oily residue extracted with ether. The extract was washed successively with 2*N*-sodium carbonate, water, 2*N*-hydrochloric acid, and water. After being dried (Na_2SO_4), the ethereal solution was evaporated and the residue chromatographed through alumina (60 g.). Elution with light petroleum–benzene gave unchanged starting material (620 mg.). Elution with ether–chloroform mixtures and with chloroform, followed by crystallisation from methanol, gave plates (476 mg.), m. p. 246—248°, $[\alpha]_D^{25}$ + 18·1° ± 3° (*c*, 4·529 in chloroform) (Found : C, 70·3; H, 9·3. Calc. for $C_{29}H_{44}O_3$: C, 70·4; H, 9·2%), shown to be 6β-acetoxy-3β : 5α-hydroxy*allo*pregnan-20-one (X) by comparison with the substance described by Ehrenstein and Stevens (*J. Org. Chem.*, 1941, **6**, 908), who give $[\alpha]_D^{20}$ + 11·8° in acetone. Elution with chloroform–methanol (20 : 1), followed by repeated crystallisation from methanol, gave prisms (550 mg.), m. p. 250—253° (Found : C, 71·7; H, 9·9. Calc. for $C_{21}H_{34}O_4$: C, 72·0; H, 9·8%), identified as 3β : 5α : 6β-trihydroxy*allo*pregnan-20-one (XI) by comparison with the substance described by Ehrenstein and Stevens (*loc. cit.* ; *J. Org. Chem.*, 1939, **4**, 506).

Derivatives.—A solution of (X) (0·1 g.) in pyridine (2 ml.) and acetic anhydride (1 ml.) was kept for 18 hours at room temperature and then evaporated under reduced pressure. An ethereal extract of the

residue was washed till neutral and dried (Na_2SO_4) and after crystallisation from methanol gave the 3β : 6β-diacetate (XIII) (88 mg.; m. p. 215—217°; $[\alpha]_D^{17}$ −12·2° ± 3° (*c*, 3·283 in chloroform); Ehrenstein and Stevens (*J. Org. Chem.*, 1940, **5**, 318) give $[\alpha]_D^{20}$ −2·0° in acetone). When similarly treated, (IX) (0·1 g.) gave (XIII) (95 mg.), m. p. 215—217° (not depressed on admixture with the substance obtained from (X)) $[\alpha]_D^{17}$ −10·8° ± 2° (*c*, 1·016 in acetone) (Found: C, 68·9; H, 8·8. Calc. for $C_{33}H_{54}O_6$: C, 69·1; H, 8·8%).

Hydrolysis of (X) (100 mg.) with potassium hydroxide (100 mg.) in boiling methanol (2 ml.) and water (0·3 ml.) for 2 hours, addition of water (5 ml.), and removal of the methanol under reduced pressure gave a residue which was extracted with ether. Isolation as usual and crystallisation from methanol gave (XI), m. p. 250—253°, not depressed on admixture with the substance obtained directly by irradiation.

Oxidation of (X) (40 mg.) according to Ehrenstein and Stevens' method (*J. Org. Chem.*, 1941, **6**, 908) gave (XII) (29 mg.) as prisms, m. p. 216—217° (from alcohol) in agreement with their data.

Optical rotations were kindly measured by Drs. A. Ruff and R. Casanova at University College, Swansea, to whom our thanks are offered. The values agreed with those given in the literature except for (X) and (XIII) (see above); the reason for these differences, which are beyond experimental error, is not clear. M.p.s are uncorrected. Microanalysis were by Drs. Weiler and Strauss (Oxford).

Our thanks are offered to the Medical Research Council for a maintenance grant for one of us (M. K.), and to the Northern Council of the British Empire Cancer Campaign for financial support. We are greatly indebted to Dr. F. T. Farmer and Mr. M. Day for their assistance with the *X*-irradiations.

KING'S COLLEGE, UNIVERSITY OF DURHAM, NEWCASTLE-UPON-TYNE. [*Received, June 9th*, 1950.]

---

521. *The Copper-catalysed Decomposition of Aliphatic Diazo-compounds: The Formation of Paraffins of High Molecular Weight.*

By G. D. BUCKLEY, L. H. CROSS, and N. H. RAY.

The copper-catalysed decomposition of a series of aliphatic diazo-compounds in ethereal solution has been studied. Diazomethane gives *ca.* 10% of polymethylene, a straight-chain, highly crystalline paraffin of high molecular weight. Diazoethane gives almost quantitative yields of polyethylidene, a hard brittle glass, and 1-diazopropane gives the very similar polypropylidene. 1-Diazobutane gives only but-1-ene, and secondary and higher primary diazo-compounds give only simple ketazines and aldazines.

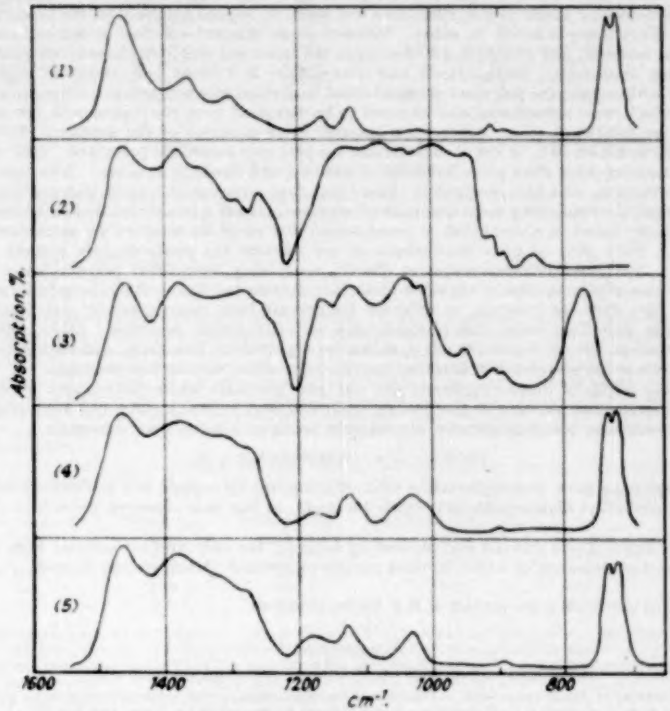
Interpolymers have been prepared by the decomposition of mixtures of diazomethane and diazoethane. With small proportions of diazoethane the products are crystalline waxes, but higher proportions of diazoethane yield amorphous glasses.

HAMBERGER and TCHIRNER (*Ber.*, 1900, **33**, 956) observed that on long storage ethereal solutions of diazomethane deposit a white precipitate which has the composition $[CH_2]_x$ (cf. also Meerwein, Rathjen, and Werner, *Ber.*, 1942, **75**, 1610). Copper and its salts have been shown to catalyse the decomposition of certain aliphatic diazo-compounds with the production of olefins (Loose, *J. pr. Chem.*, 1909, **79**, 507; Lorey, *ibid.*, 1930, **124**, 185); thus diazoacetic ester gives fumaric ester, and ω-diazotoluene gives stilbene on treatment with copper or anhydrous copper sulphate. Leitch and Cambron ("National Research Council of Canada Review," 1948, p. 94) found that copper powder catalysed the decomposition of solutions of diazomethane and diazodideuteromethane to give much improved yields of polymethylene and polydeuteromethylene, respectively.

The decomposition of a series of aliphatic diazo-compounds has now been studied. Polymethylene, prepared from diazomethane by Leitch and Cambron's method (*loc. cit.*), was a brittle crystalline wax, m. p. 135°, of molecular weight *ca.* 20,000, insoluble in ether and cold hydrocarbons, though soluble in boiling benzene and toluene. Its infra-red absorption spectrum (see figure) shows bands at 721 $cm.^{-1}$ and 732 $cm.^{-1}$, characteristic of a polymethylene chain (Thompson and Torkington, *Proc. Roy. Soc.*, 1945, **184**, *A*, 3). The weak absorption at 1365 $cm.^{-1}$ is not due to the methyl but to the methylene group (R. B. Richards, private communication).

Copper and certain of its salts catalysed the decomposition of diazoethane and 1-diazopropane in ethereal solution with the production of paraffins of high molecular weight in 90—95% yield. Although a variety of substances, such as silver powder, iron powder, zinc dust, and powdered glass were found to catalyse the decomposition of an ethereal solution of diazoethane, only copper powder, anhydrous cupric sulphate, cupric oxide, and cuprous cyanide induced the formation of paraffins of high molecular weight in good yield. Other copper compounds gave traces of these polymers. The presence of ethyl ether was also essential, since solutions of diazoethane in toluene, hexane, or tetrahydrofuran were decomposed only very slowly by copper powder, and did not give polymers. However, on addition of ether to such a reaction mixture

a more vigorous decomposition occurred and a polymer was formed. The polymers from diazoethane and diazopropane remained dissolved in the ether, in contrast to polymethylene, which was precipitated gradually as the decomposition proceeded. The products were brittle amorphous glasses, m. p. 80—100°, soluble in ether and cold hydrocarbons, but insoluble in alcohol. Analysis showed that they were hydrocarbons of empirical formula $[CH_2]_n$, and their infra-red absorption spectra (see figure) were consistent with the structures of polyethylidene and polypropylidene.



(1) *Polymethylene from diazomethane.*
(2) *Polyethylidene from diazoethane.*
(3) *Polypropylidene from diazopropane.*
(4) *Ether-insoluble interpolymer No.* 1 *containing* 3·0 *moles* % *of diazoethane.*
(5) " " " " 2 " 6·7 " " "

The spectrum of the product from diazoethane showed no bands in the 720- and 730-cm.$^{-1}$ regions, indicating absence of a polymethylene chain, and strong absorption at about 1380 cm.$^{-1}$, indicating a high concentration of methyl groups (Thompson and Torkington, *loc. cit.*). There was a series of very strong bands in the region 940—1125 cm.$^{-1}$; the 1125-cm.$^{-1}$ band is commonly found in paraffins containing adjacent methyl groups (Thompson, *J.*, 1948, 328), and the spectrum of 2 : 3 : 4-trimethylpentane, for example, shows several absorptions in this region ("Amer. Petr. Inst. Research Project 44, Nat. Bur. Standards, Catalogue of infra-red spectral data," serial No. 666) though of much lower intensity.

The spectrum of the product from 1-diazopropane was superficially similar except for an intense band at 785 cm.$^{-1}$, indicating the presence of ethyl groups (Thompson, *J.*, 1948, 328) and suggesting that this hydrocarbon is a homologue of polyethylidene. The molecular weights

of these hydrocarbons were determined, where possible, by the cryoscopic method, benzene being used as solvent. This was unsatisfactory, however, for molecular weights above 3000, and for such cases the intrinsic viscosity was measured in diisobutene at 20°. The relation $[\eta] = 1{\cdot}08M^{0{\cdot}7} \times 10^{-4}$ (Oakes and Richards, *J.*, 1949, 2929) which is used for polythene and polymethylene was clearly not applicable to polyethylidene and polypropylidene; instead the relation $[\eta] = 3{\cdot}60M^{0{\cdot}64} \times 10^{-4}$ (Flory, *J. Amer. Chem. Soc.*, 1943, **65**, 372) which holds for polyisobutene, was used as being the best available approximation. The combination of these two methods showed that the polymers ranged in molecular weight from 2,000 to 14,000.

The molecular weight of polyethylidene was found to depend inversely on the concentration of the diazoethane solution in ether. Dilution of an ethereal solution of diazoethane with benzene, however, had no significant effect upon the molecular weight of the polymer produced.

When mixtures of diazomethane and diazoethane in various proportions in ether were treated with copper, the polymers obtained could be divided into two groups: those insoluble in ether, which were precipitated and required to be extracted from the copper with hot toluene, and those soluble in ether, which were isolated on evaporation of the solution. When the mixture contained 10% or less of diazoethane the polymers resembled polythene; they were of higher melting-point than polyethylidene, crystalline, and insoluble in ether. Although ether-soluble fractions were also obtained in these cases, they were not polymeric hydrocarbons, but oily impurities containing large amounts of nitrogen; small amounts of similar bodies were occasionally found in polyethylidene preparations and could be removed by extraction with alcohol. With 40% or more diazoethane in the mixture the products were entirely ether-soluble; they were brittle amorphous glasses, resembling unmodified polyethylidene. The infra-red absorption spectra of the ether-insoluble polymers (see figure) showed small absorptions in the 950—1200-cm.$^{-1}$ region, at different frequencies from those given by polyethylidene, indicating that they were true interpolymers and not simple mixtures. There were new absorptions at 721 cm.$^{-1}$ and 732 cm.$^{-1}$, indicating a polymethylene chain, and their intensities diminished as the proportion of diazomethane in the reaction mixture was reduced.

Higher aliphatic diazo-compounds did not give polymers when decomposed by copper. 1-Diazobutane lost nitrogen to give mainly but-1-ene, and 1-diazopentane and 1-diazoheptane gave valeraldazine and heptaldazine, respectively, losing only half of their nitrogen:

$$2RCHN_2 \longrightarrow RCH{:}N{\cdot}N{:}CHR + N_2$$

2-Diazopropane gave dimethylketazine when decomposed by copper, but ω-diazotoluene gave stilbene and ethyl diazoacetate gave ethyl fumarate, as has been observed previously (Loose, *loc. cit.*).

3-Diazoprop-1-ene was not decomposed by copper; the only product isolated from it was pyrazole, the formation of which involves no loss of nitrogen (Adamson and Kenner, *J.*, 1935, 286).

Part of this work is the subject of B.P.Appln. 26313/49.

Experimental.

(Microanalyses are by Dr. A. F. Colson. All m. p.s are corrected.)

Preparation of Diazo-compounds.—Diazomethane, diazoethane, and 1-diazopropane were prepared from the methyl *N*-nitroso-2-alkylaminoisobutyl ketones as described by Jones and Kenner (*J.*, 1933, 363) and Adamson and Kenner (*loc. cit.*). It was found advisable to use the nitroso-ketones shortly after they had been made, otherwise poor yields of diazo-compounds were obtained. 1-Diazobutane, 1-diazopentane, and 1-diazoheptane were prepared from the corresponding nitrosoureas, and 2-diazopropane by oxidation of acetone hydrazone with mercuric oxide (Staudinger and Gaule, *Ber.*, 1916, **49**, 1905).

Molecular-weight Determinations.—The molecular weights of polymethylene and of the ether-insoluble interpolymers from diazomethane and diazoethane were calculated from their intrinsic viscosities measured in tetralin at 75°, the equation $[\eta] = 1{\cdot}08M^{0{\cdot}7} \times 10^{-4}$ (Oakes and Richards, *loc. cit.*) being used. See also above.

Infra-red Absorption Spectra.—The instrument used was a Grubb Parsons, model S.3, single-beam infra-red recording spectrometer; 0·15 mm. thick films between rock-salt plates were used throughout, and the cell compartment was kept at 28° ± 2°. The effective slit widths were 11 cm.$^{-1}$ at 6μ., 6 cm.$^{-1}$ at 10μ., and 3 cm.$^{-1}$ at 14μ.

Decomposition of Diazomethane.—Copper powder (1 g.) was added to a solution of diazomethane (4·6 g.) in ether (200 c.c.). Nitrogen was evolved slowly and after 24 hours the solution was colourless and contained a white flocculent precipitate. The precipitate, together with the copper, was collected and, after being dried *in vacuo* at 60°, was extracted with boiling xylene. The cooled extract was diluted with twice its volume of methanol, giving polymethylene (0·15 g.), m. p. 132°, *M ca.* 20,000, d_4^{20} 0·965 (Found: C, 85·6; H, 14·1. Calc. for $(CH_2)_n$: C, 85·7; H, 14·3%).

Decomposition of Diazoethane.—Copper powder (1 g.) was added to a solution of diazoethane (3·4 g.) in dry ether (500 c.c.). Nitrogen was slowly evolved and the solution was colourless after 21 hours; it was filtered and evaporated to dryness, and the residue was washed with ethanol and dried at 100°/3 mm. The product (1·5 g.) was a pale yellow, brittle glass, m. p. 90—100°, d_4^{20} 0·909, [η] 0·088, *M*, 5800 (Found: C, 85·7; H, 14·3. $[C_2H_4]_n$ requires C, 85·7; H, 14·3%). The infra-red absorption spectrum showed it to be a *polyethylieneā* (see figure). The experiment was repeated, various catalysts being used, with the following results:

Catalyst.*	Reaction time.	Yield of polymer, g.	*M*.	Remarks.
Silver powder	24 hours	nil	—	—
Iron powder	2 days	nil	—	—
Zinc dust	3 days	nil	—	—
Cupric sulphate	5 mins.	1·5	7200	Very vigorous reaction
Cupric nitrate	<1 min.	trace	—	Violent reaction
Cupric acetate	<1 min.	trace	—	Violent reaction
Cuprous cyanide ...	5 mins.	1·5	2500	Vigorous reaction
Cupric oxide	2 days	0·7	500	Liquid product
Cuprous oxide	1 hour	trace	—	—
Powdered glass	3 days	nil	—	Very slow and incomplete reaction

* All salts were anhydrous.

Effect of Concentration.—Diazoethane solutions of various concentrations (each containing 1·04 g. of diazoethane) were treated with copper powder (1 g.) and the products isolated as described above. The effect of concentration on molecular weight is:

Concentration, g./l.	3·4	6·2	10·4
[η]	0·163	0·087	0·051
M	14,000	5,400	2,300

Effect of Other Solvents.—Solutions of diazoethane in toluene, hexane, and tetrahydrofuran were prepared by decomposing methyl *N*-nitroso-2-ethylaminoisobutyl ketone in anisole with sodium *cyclo*hexyloxide (Adamson and Kenner, *J.*, 1937, 1551) and collecting the diazoethane in a wash-bottle containing the selected solvent cooled in "Drikold." Addition of copper powder to these solutions produced a slow evolution of nitrogen and the colour was discharged in 24 hours. After filtering off the copper and evaporating to dryness there was in each case only a trace of oily residue. To a solution of diazoethane (1 g.) in toluene (200 c.c.) was added ether (10 c.c.) and copper powder (0·5 g.). A more vigorous evolution of gas took place, the colour was discharged in 10 hours and polyethylidene (0·3 g.) was isolated as described above.

A number of ethereal diazoethane solutions were diluted with varying amounts of dry benzene, and treated with copper powder (2 g.). The results were:

Diazoethane, g.	Ether, c.c.	Benzene, c.c.	Diazoethane concentration, g./l.	Product, [η].	Product, *M*.
5·2	200	nil	26	0·070	3900
5·2	200	100	17·3	0·089	5600
5·2	200	200	13	0·073	4000
5·2	200	400	8·7	0·072	4000
5·2	200	800	5·2	0·090	5600

Decomposition of 1-Diazopropane.—Copper powder (1 g.) was added to a solution of 1-diazopropane (2·4 g.) in ether (260 c.c.). Nitrogen was evolved rapidly, and after 50 minutes the solution was colourless. The copper was removed by filtration and the solution evaporated to dryness, leaving *polypropylidene* (1·4 g.) as a pale yellow, brittle glass, m. p. 80—96°, [η] 0·105, *M* 7,000 (Found: C, 85·7; H, 14·3%). Its infra-red absorption spectrum is shown in the figure.

Decomposition of 2-Diazopropane.—Anhydrous copper sulphate (0·2 g.) was added to a solution of 2-diazopropane (0·44 g.) in ether (100 c.c.). The colour was discharged in 5 minutes, and the solution was filtered and evaporated; the residue was distilled giving dimethyl ketazine (0·3 g.), b. p. 130—131° (Found: C, 64·0; H, 10·5; N, 24·9%; *M*, 114. Calc. for $C_6H_{12}N_2$: C, 64·3; H, 10·7; N, 25·0%; *M*, 112).

Decomposition of 1-Diazobutane.—Copper powder (2 g.) was added to a solution of 1-diazobutane (3·5 g.) in ether (200 c.c.) in a flask connected to a liquid-air trap. A rapid evolution of gas took place and the reaction was complete in 10 minutes. The trap contained but-1-ene, b. p. −6°, and ether. The solution left in the flask was filtered and evaporated to dryness, leaving only a trace of oily residue.

Decomposition of 1-Diazopentane.—Copper powder (0·3 g.) was added to a solution of 1-diazopentane (1 g.) in ether (40 c.c.); there was an immediate reaction. The solution was filtered and evaporated, and the residue was distilled under reduced pressure to give *valeraldazine* (0·3 g.), b. p. 100°/2·5 mm (Found: C, 71·4; H, 11·7; N, 16·5. $C_{10}H_{20}N_2$ requires C, 71·4; H, 11·9; N, 16·7%). On treatment with Brady's reagent, valeraldehyde 2:4-dinitrophenylhydrazone, m. p. 98°, was obtained (Found: C, 50·6; H, 5·1; N, 20·8. Calc. for $C_{11}H_{14}O_4N_4$: C, 49·6; H, 5·3; N, 21·0%).

Decomposition of 1-Diazoheptane.—Anhydrous copper sulphate (0·1 g.) was added to a solution of 1-diazopheptane (5 g.) in ether (350 c.c.) (Chao-Lun Tseng and Teh-Sen Ho, *J. Chinese Chem. Soc.*, 1936, **4**, 335). There was an immediate and violent effervescence, and the solution became black. It was treated with charcoal and filtered, and the filtrate evaporated. The residue (4·8 g.) was distilled, giving

heptan-1-ol (0·5 g.), b. p. 175—180° (Found : C, 72·5; H, 13·2. Calc. for $C_7H_{15}O$: C, 72·4; H, 13·8%), and heptaldazine (3·5 g.), b. p. 158—164°/21 mm. (Found : C, 74·5; H, 12·2; N, 12·3. Calc. for $C_{14}H_{28}N_2$: C, 75·0; H, 12·5; N, 12·5%), which on treatment with Brady's reagent gave heptaldehyde 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 107·5°. In addition a small fraction boiled at 180—185°/10 mm. and deposited crystals on storage ; after recrystallisation from ether these had m. p. 90° but could not be identified (Found : C, 68·7; H, 10·7; N, 11·1%).

Interpolymers from Diazomethane and Diazoethane.—Ethereal solutions containing varying proportions of diazomethane and diazoethane were treated with copper powder (2 g.) and left until colourless. The solutions were filtered ; the copper residues were extracted with boiling toluene, and the extract evaporated to dryness to isolate the ether-insoluble polymer fractions ; the filtered ethereal solutions were also evaporated, giving the ether-soluble fractions. The following results were obtained :

					Products,					
					ether-soluble,			ether-insoluble,		
No.	Diazomethane, g.	Diazoethane, g.	Ether, c.c.	Diazoethane, moles %	yield, g.	m. p.	*M.*	yield, g.	m. p.	*M.*
1	7·3	0·3	700	3·0	0·5	viscous	—	0·5	113°	3800
2	6·2	0·6	635	6·7	0·5	liquids	—	0·3	108	3900
3	3·1	2·9	638	41·2	1·3	70°	4000	nil	—	—
4	0·7	5·8	640	86·3	1·7	85	5000	nil	—	—

The ether-soluble fractions from Nos. 1 and 2 were also soluble in alcohol and contained large quantities of nitrogen ; they were not investigated further. The two ether-insoluble fractions were white brittle waxes, insoluble in cold hydrocarbons, and showed *X*-ray diffraction patterns typical of crystalline compounds ; their infra-red absorption spectra are shown in the figure. The ether-soluble fractions Nos. 3 and 4 were amorphous glasses, very similar to unmodified polyethylidene, soluble in cold hydrocarbons but not in alcohol.

The authors are indebted to Dr. A. Cambron for a specimen of polymethylene and for information on the decomposition of diazomethane by copper.

IMPERIAL CHEMICAL INDUSTRIES LIMITED, RESEARCH DEPARTMENT,
ALKALI DIVISION, NORTHWICH, CHESHIRE. [*Received, May 22nd*, 1950.]

---

522. *Insecticidal Activity and Chemical Constitution. Part II. Synthesis of Some Analogues of "DDT."*

By E. JOHN SKERRETT and D. WOODCOCK.

Several analogues of DDT have been synthesised. All showed little or no activity when tested as contact insecticides against *Calandra granaria*, L.

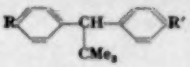
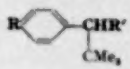
SINCE the discovery of the outstanding insecticidal activity of 1 : 1 : 1-trichloro-2 : 2-di-*p*-chlorophenylethane (DDT), many related compounds have been synthesised and some correlation between chemical structure and toxicity is apparent ; *e.g.*, Busvine (*J. Soc. Chem. Ind.*, 1946, **65**, 356), after examining 41 DDT analogues, emphasised that the most toxic were most similar to DDT in shape and weight, a conclusion also reached by Prill, Synerholm, and Hartzell [*Contr. Boyce Thompson Inst.*, 1946, **14**, (6), **341**] in connection with the *p*-substituents, and by Fleck (*J. Amer. Chem. Soc.*, 1948, **70**, **2173**). Campbell and West (*Chem. and Ind.*, 1945, **334**) suggested that the three β-chlorine atoms were necessary for optimal toxicity owing to a certain steric orientation requirement which also involved the nuclear chlorine atoms in the *p*-positions for maximum effect. Replacement of two or more of the β-chlorine atoms generally has an adverse effect on toxicity.

If the toxicity of DDT is due to its structural resemblance to some essential insect metabolite, then isosteres should presumably act similarly, and replacement of the three β-chlorine atoms by spatially similar atoms or groups of atoms should not destroy activity. The dimensions of the hydroxyl group (radius 1·7 A.) and the methyl group (radius 2·0 A.) agree reasonably well with those of the chlorine atom (radius 1·8 A.) and there are several reported cases of the biological equivalence of CH_3 and Cl. Thus Kuhn and his co-workers (*Ber.*, 1943, **76**, 1044) found that 6 : 7-dichloro-9-ribitylisoalloxazine effectively interferes with the action of 6 : 7-dimethyl-9-ribitylisoalloxazine (riboflavin) so that the growth of certain bacterial species is prevented. This degree of structural conformity has also been shown by Pauling and Pressman (*J. Amer. Chem. Soc.*, 1945, **67**, 1003) to be well within the limits required for isosteric activity in serological reactions.

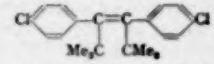
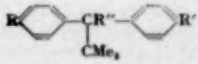
$CO_2H{\cdot}CH(C_6H_4Cl)_2$ (I.) $COMe{\cdot}CH(C_6H_4Cl)_2$ (II.) $C(OH)_2{\cdot}CH(C_6H_4Cl)_2$ (III.) $CMe(OH)_2{\cdot}CH(C_6H_4Cl)_2$ (IV.)

Erlenmeyer, Bitterli, and Sorkin (*Helv. Chim. Acta*, 1948, **31**, 466) postulated that the compounds (I) and (II) might function biologically as the corresponding tri- (III) and di-hydroxymethyl (IV) compounds. Tested against *Musca domestica*, *Tinea granella*, and *Dermestes frischii*, both were inactive, though potentially at least isosteric with DDT. However, it is known that whilst replacement of the chlorine atoms in the *p*-positions of DDT by methyl groups reduces the toxicity somewhat, the effect of replacement of the chlorine atoms by polar but lipophobic hydroxyl groups is to produce a compound virtually devoid of insecticidal properties (Martin and Wain, *Ann. Rep. Agric. Hort. Res. Sta., Long Ashton*, 1944, p. 121).

It was thought therefore to be of interest to prepare a series of compounds involving substitution of methyl groups for the chlorine atoms in the DDT molecule. Of the two obvious routes to the structure (V; R = R′ = Cl), that employing the carbinol (VI; R = Cl, R′ = OH) was preferred to the Baeyer condensation using the more difficultly accessible trimethylacet-

(V.)  

aldehyde. Treatment of *tert.*-butylmagnesium chloride with *p*-chlorobenzaldehyde usually gave a product containing varying amounts of *p*-chlorobenzyl alcohol (cf. Hess and Rheinbolt, *Ber.*, 1921, **54**, 2043; 1924, **57**, 1921), but by carrying out the reaction at *ca.* −30° 1-*p*-chlorophenyl-2 : 2-dimethylpropan-1-ol (VI; R = Cl, R′ = OH) was obtained in 55% yield. Attempts to condense this carbinol with chlorobenzene in the presence of concentrated sulphuric acid and oleum failed to give the required substance (V; R = R′ = Cl). A compound, m. p. 127°, isolated from the distillate was probably (VII).

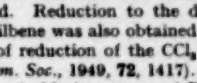
(VII.)   (VIII.)

Condensation of *p*-chlorophenylmagnesium bromide with methyl trimethylacetate, however, gave 1 : 1-di-*p*-chlorophenyl-2 : 2-dimethylpropan-1-ol (VIII; R = R′ = Cl, R″ = OH) which in ethyl-alcoholic solution was smoothly reduced by means of amalgamated zinc and dry hydrogen chloride to 1 : 1-di-*p*-chlorophenyl-2 : 2-dimethylpropane (V; R = R′ = Cl). The pentamethyl analogue of DDT (V; R = R′ = Me) was prepared similarly from 1 : 1-di-*p*-tolyl-2 : 2-dimethylpropan-1-ol (VIII; R = R′ = Me, R″ = OH) which had been obtained from *p*-tolylmagnesium bromide.

Oxidation of 1-*p*-chlorophenyl-2 : 2-dimethylpropan-1-ol (VI; R = Cl, R′ = OH) with chromic acid and reaction of the resulting ketone with *p*-tolylmagnesium bromide gave the asymmetrical carbinol (VIII; R = Cl, R′ = CH_3, R″ = OH) which was reduced to the hydrocarbon (V; R = Cl, R′ = CH_3) as already described for the symmetrical compounds.

During preliminary work the reaction of DDT and some of its analogues with methylmagnesium iodide was examined. Reduction to the dichloroethane was general, and from DDT itself some 4 : 4′-dichlorostilbene was also obtained (cf. Forrest, Stephenson, and Waters, *J.*, 1945, 333). A similar case of reduction of the CCl_3 group has recently been reported by Pepper and Kulka (*J. Amer. Chem. Soc.*, 1949, **72**, 1417).

Successive replacement of the β-chlorine atoms of DDT by methyl groups would lead to compounds (IX) and (X; R = R′ = R″ = Cl). An obvious route to the dichloro-compound



$CMeCl_2{\cdot}CH(C_6H_4Cl)_2$ (IX.) (X.) $CHMe(OH){\cdot}C(OH)(C_6H_4Cl)_2$ (XI.)

(IX) requires 1 : 1-di-*p*-chlorophenylacetone. Attempts to prepare this compound from di-*p*-chlorophenylacetonitrile were not successful, neither methylmagnesium iodide nor methyllithium showing any tendency to react (cf. Gilman and Kirby, *J. Amer. Chem. Soc.*, 1933, **55**, 1270).

Reaction between *p*-chlorophenylmagnesium bromide and ethyl lactate, however, gave the diol (XI), but removal of the elements of water by refluxing this with acetic anhydride, to give the enolic form of 1 : 1-di-*p*-chlorophenylacetone as described by Stoermer (*Ber.*, 1906, **39**, 2288), could not be achieved; acetic anhydride in the presence of fused sodium acetate gave the diol acetate in the usual way. Finally, 1 : 1-di-*p*-chlorophenylacetone was obtained as a

crystalline solid, m. p. 52—53°, by hydrolysis of the condensation product from sodiomalonic ester and di-*p*-chlorophenylacetyl chloride (cf. Erlenmeyer *et al.*, *loc. cit.*). It appeared stable to 2*N*-sodium hydroxide and the large amounts of 4 : 4′-dichlorobenzophenone isolated in some experiments were probably formed by autoxidation of the intermediate β-keto-γγ-di-*p*-chlorophenyl-*n*-butyric acid (cf. Rigaudy, *Compt. rend.*, 1949, **228**, 253). Treatment with phosphorus pentachloride over a wide range of reaction temperatures gave the chloroethylene (XII; R = Cl) as the main product. If this is formed *via* the enol, the stability of 1 : 1-di-*p*-chlorophenylacetone to alkali is surprising in view of Rigaudy's results (*loc cit.*).

Ethyl di-*p*-chlorophenylacetate reacted smoothly with methylmagnesium iodide, forming the carbinol (X; R = R′ = Cl, R″ = OH) in 92% yield. Treatment with phosphorus pentachloride at room temperature gave 2-chloro-1 : 1-di-*p*-chlorophenyl-2-methylpropane (X; R = R′ = R″ = Cl), a viscous liquid which was readily dehydrochlorinated by boiling alcoholic sodium hydroxide to give 1 : 1-di-*p*-chlorophenyl-2-methylprop-1-ene (XII; R = Me), m. p. 69—70°. It is suggested that the chloro-compound (X; R = R′ = R″ = Cl) results

$$CRMe{:}C(C_6H_4Cl)_2 \qquad CH_2{:}CMe{\cdot}CH(C_6H_4Cl)_2$$
(XII.) (XIII.)

from the decomposition of an intermediate phosphorus-containing complex by the sodium hydrogen carbonate used in the isolation procedure. When the carbinol was treated with phosphorus pentachloride at temperatures above 100°, 1 : 1-di-*p*-chlorophenyl-2-methylprop-2-ene (XIII), m. p. 124°, was obtained in addition to the isomer (XII; R = Me). In this case breakdown of the phosphorus complex is postulated to yield both ethylenes without previous formation of 2-chloro-1 : 1-di-*p*-chlorophenyl-2-methylpropane (X; R = R′ = R″ = Cl) since the latter has been shown to be stable to phosphorus pentachloride at 140°.

The structures of the isomers (XII; R = Me) and (XIII) were assigned after oxidation by means of chromic acid had been carried out in a stream of carbon dioxide. The higher-melting isomer (XIII) gave formaldehyde, and the lower-melting (XII; R = Me) formed acetone, both isolated as their 2 : 4-dinitrophenylhydrazones. Confirmation of formula (XII;

$$[(Cl{\cdot}C_6H_4)_2CH{\cdot}CMe_2]_2O \qquad CR'(CHR_2)(C_6H_4Cl)_2$$
(XIV.) (XV.)

R = Me) was obtained by an unambiguous synthesis. Interaction of ethyl *iso*butyrate and *p*-chlorophenylmagnesium bromide afforded 1 : 1-di-*p*-chlorophenyl-2-methylpropan-1-ol (XV; R = Me, R′ = OH), which was readily converted into (XII; R = Me) by treatment with potassium hydrogen sulphate at 160°. Some early attempts to obtain an ethylene from the carbinol (X; R = R′ = Cl, R″ = OH) by means of potassium hydrogen sulphate at 170—180° gave the ether (XIV).

Replacement of one chlorine atom of the CCl_3 group of DDT by hydrogen leads to 1 : 1-dichloro-2 : 2-di-*p*-chlorophenylethane (DDD) (XV; R = Cl, R′ = H) which still possesses moderate insecticidal activity (Cristol *et al.*, *Science*, 1946, **104**, 343; Busvine, *loc. cit.*; Stringer, *Ann. Appl. Biol.*, 1949, **36**, 206). The isosteric compound (XV; R = Me, R′ = H) obtained by catalytic reduction of either (XII; R = Me) or (XIII) had no such activity.

The seven analogues (V; R = R′ = Cl; R = R′ = Me; R = Cl, R′ = Me) and (X; R = R′ = Cl, R″ = OH; R = R′ = Me, R″ = OH; R = R′ = R″ = Cl; R = R′ = Me, R″ = Cl) which have been prepared showed little or no activity when tested by Mr. A. Stringer as contact insecticides against *Calandra granaria*.* It is suggested that the difference between these and DDT is caused by some intrinsic property of the CCl_3 group, probably its capacity for electron attraction. That 2-chloro-1 : 1-di-*p*-chlorophenyl-2-methylpropane (X; R = R′ = R″ = Cl) is also non-insecticidal though readily capable of losing hydrogen chloride, is also significant in view of Martin and Wain's suggestion (*Nature*, 1944, **154**, 512) that ready dehydrochlorination is a prerequisite of insecticidal activity.

Experimental.

(M.p.s are uncorr. C and H microanalyses are by Drs. Weiler and Strauss.)

1-*p*-Chlorophenyl-2 : 2-dimethylpropan-1-ol (VI; R = Cl, R′ = OH).—A dry ethereal solution of *tert.*-butylmagnesium chloride, prepared from *tert.*-butyl chloride (46·7 ml.) and magnesium turnings (10·4 g.), was cooled to below −30° (solid carbon dioxide–acetone) and vigorously stirred during the

* [*Added in proof.*] Brown and Rogers (*J. Amer. Chem. Soc.*, 1950, **72**, 1864) reported that the DDT isostere (V; R = R = OMe) possesses considerable insecticidal activity against several species. Prepared by us this compound was completely non-toxic to *Calandra granaria* L.

cautious dropwise addition of *p*-chlorobenzaldehyde (14 g.) dissolved in ether (25 ml.). After a further 4—5 hours' stirring at the same temperature, the reaction mixture was decomposed with 2*N*-sulphuric acid and extracted with ether. The extract, after being washed with water, saturated sodium hydrogen sulphite (three times), and sodium hydrogen carbonate, was dried, and the solvent removed. Distillation of the residue gave 1-p-*chlorophenyl*-2 : 2-*dimethylpropan*-1-*ol* as a colourless liquid (10·9 g., 55%), b. p. 90—95°/0·5 mm., n_D^{14} 1·5401 (Found : C, 66·7; H, 7·7; Cl, 17·9. $C_{11}H_{14}OCl$ requires C, 66·5; H, 7·6; Cl, 17·9%). Treatment with phenyl isocyanate in light petroleum (b. p. 80—100°) gave the *phenylurethane*, which crystallised from aqueous methanol in colourless rhombic prismatic plates, m. p. 129° (Found : C, 68·1; H, 6·3; Cl, 11·2. $C_{18}H_{20}O_2NCl$ requires C, 68·0; H, 6·3; Cl, 11·2%). When the above reaction was carried out with only ice-cooling, the final distillate generally partly solidified. The solid, m. p. 72—73°, was identified as *p*-chlorobenzyl alcohol by mixed m. p. with an authentic specimen, and by the preparation of the *phenylurethane*, which crystallised from light petroleum (b. p. 80—100°) in colourless monoclinic prisms, m. p. 93·5° (Found : C, 64·5; H, 4·6; Cl, 13·9. $C_{14}H_{12}O_2NCl$ requires C, 64·3; H, 4·6; Cl, 13·6%). Attempts to separate the carbinol (VI; R = Cl, R′ = OH) and *p*-chlorobenzyl alcohol by fractionation of the acetylated mixture were unsuccessful.

1-*Chloro*-1-p-*chlorophenyl*-2 : 2-*dimethylpropane* (VI; R = R′ = Cl).—A solution of the carbinol (VI; R = Cl, R′ = OH) (4·8 g.) in dry benzene (10 ml.) was added cautiously with shaking to a suspension of phosphorus pentachloride (6·0 g., 1·2 mols.) in dry benzene (10 ml.). After being heated at 100° for 0·25 hour the mixture was diluted with water and extracted with ether, the extract dried, and the solvent removed. Distillation of the residue gave a colourless mobile liquid (4·5 g.), b. p. 80—84°/0·4 mm., n_D^{15} 1·5372 (Found : Cl, 33·0. $C_{11}H_{14}Cl_2$ requires Cl, 32·7%).

1 : 1-*Di*-p-*chlorophenyl*-2 : 2-*dimethylpropan*-1-*ol* (VIII; R = R′ = Cl, R″ = OH).—(*a*) *tert.*-Butylmagnesium chloride, prepared from *tert.*-butyl chloride (11·5 g.) and magnesium clippings (3 g.), was refluxed with di-*p*-chlorophenyl ketone (10 g.) in absolute ether (50 ml.) for 1 hour. After cooling and decomposition with 2*N*-sulphuric acid the product on isolation consisted of unchanged ketone and a little di-*p*-chlorophenylcarbinol.

(*b*) *p*-Chlorophenylmagnesium bromide, prepared from *p*-chlorobromobenzene (38·3 g.) and magnesium turnings (4·8 g.), was vigorously stirred in anhydrous ether (75 ml.) at 0° during the slow dropwise addition of methyl pivalate (11·6 ml.) in anhydrous ether (25 ml.). After refluxing for 16 hours, the reaction mixture was cooled in ice and decomposed with 2*N*-sulphuric acid. Extraction with ether and distillation of the product left after removal of the dried solvent gave unchanged chlorobromobenzene (3·6 g.) and the tertiary *carbinol* (VIII; R = R′ = Cl, R″ = OH) as a colourless viscous liquid (16·8 g., 54%), b. p. 160—164°/0·4 mm., n_D^{15} 1·5924 (Found : C, 66·2; H, 5·8; Cl, 23·2. $C_{17}H_{18}OCl_2$ requires C, 66·0; H, 5·8; Cl, 23·0%). Attempts to acetylate this and to form its phenyl- and α-naphthylurethanes were unsuccessful. Oxidation in glacial acetic acid with chromic acid gave 4 : 4′-dichlorobenzophenone, m. p. 145—146°, undepressed on admixture with an authentic specimen.

1-*Chloro*-1 : 1-*di*-p-*chlorophenyl*-2 : 2-*dimethylpropane* (VIII; R = R′ = R″ = Cl).—The carbinol (VIII; R = R′ = Cl, R″ = OH) (4·0 g.) failed to react with phosphorus pentachloride (3 g., 1 mol.) at 100°, but when heated at 140° for 2 hours afforded the *trichloro*-compound which, isolated by ether, distilled as a colourless viscous liquid (2·4 g., 56%), b. p. 190—192°/0·5 mm. (Found : Cl, 30·7. $C_{17}H_{17}Cl_3$ requires Cl, 32·5%).

1 : 1-*Di*-p-*chlorophenyl*-2 : 2-*dimethylpropane* (V; R = R′ = Cl).—The carbinol (VIII; R = R′ = Cl, R″ = OH) (7·7 g.) and amalgamated zinc (30 g.) were treated in refluxing ethyl alcohol (40 ml.) with dry hydrogen chloride for 3 hours. The oily layer which had separated on the surface was isolated with ether, and the extract washed with sodium hydrogen carbonate solution and dried. Removal of the solvent and distillation of the residual oil gave the *dichloro*-compound (6·3 g., 86%), b. p. 153°/0·5 mm., n_D^{14} 1·5861 (Found : C, 70·2; H, 6·0; Cl, 24·2. $C_{17}H_{16}Cl_2$ requires C, 69·6; H, 6·1; Cl, 24·2%). Treatment with fuming nitric acid at 0° for 0·5 hour and pouring on ice gave a cream-coloured solid which was collected, washed with water, and dried in a desiccator (Found : Cl, 18·3. $C_{17}H_{15}O_4N_2Cl_3$ requires Cl, 18·5%). This product, which was very soluble in ether and methanol, could not be obtained crystalline and is probably a mixture of isomeric *dinitro*-derivatives. Attempts to form a picrate of (V; R = R′ = Cl) were unsuccessful.

3 : 4-*Di*-p-*chlorophenyl*-2 : 2 : 5 : 5-*tetramethylhex*-3-*ene* (VII).—A mixture of 1-*p*-chlorophenyl-2 : 2-dimethylpropan-1-ol (4·2 g.) and chlorobenzene (2·3 ml.) was vigorously stirred during the addition of concentrated sulphuric acid (4 ml.) and oleum (2 ml.) and for a further 5 hours, then poured on ice; the *hexene* was isolated with ether and distilled. A glassy liquid (2·7 g.), b. p. 185°/0·5 mm., was obtained which after repeated recrystallisation from ethyl alcohol gave prisms, m. p. 127° [Found : C, 73·2; H, 7·1; Cl, 19·8%; *M* (cryoscopic in benzene), 325. $C_{22}H_{26}Cl_2$ requires C, 73·1; H, 7·2; Cl, 19·7%; *M*, 361].

1 : 1-*Di*-p-*tolyl*-2 : 2-*dimethylpropan*-1-*ol* (VIII; R = R′ = Me, R″ = OH).—*p*-Tolylmagnesium bromide, prepared from *p*-bromotoluene (34·2 g.) and magnesium turnings (4·8 g.) in absolute ether (125 ml.), was treated at 0° with a solution of methyl trimethylacetate (11·6 ml.) in absolute ether (25 ml.). After refluxing for 3 hours, the reaction mixture was cooled and the *propanol* isolated as for the analogue (VIII; R = R′ = Cl, R″ = OH). It was a colourless viscous liquid (5·4 g., 31%), b. p. 162—166°/0·5 mm., n_D^{14} 1·5862 (Found : C, 85·2; H, 9·0. $C_{19}H_{24}O$ requires C, 85·1; H, 9·0%). The structure was confirmed by chromic acid oxidation in glacial acetic acid solution to 4 : 4′-dimethylbenzophenone, m. p. 94—95° undepressed on admixture with an authentic specimen.

1 : 1-*Di*-p-*tolyl*-2 : 2-*dimethylpropane* (VI; R = R′ = Me).—Treatment of the carbinol (VIII; R = R′ = Me, R″ = OH) (2·2 g.) with amalgamated zinc (10 g.) in the presence of dry hydrogen chloride, as already described for the corresponding chloro-carbinol (VIII; R = R′ = Cl, R″ = OH),

gave the *propane* as a colourless mobile liquid (1·4 g.), b. p. 120—122°/0·3 mm., n_D^{25} 1·5540 (Found: C, 90·8; H, 9·0. $C_{15}H_{24}$ requires C, 90·5; H, 9·5%).

p-Chlorophenyl tert.-Butyl Ketone.—1-*p*-Chlorophenyl-2 : 2-dimethylpropan-1-ol (VI; R = Cl, R′ = OH) was oxidised by the method of Mosher and Langerak (*J. Amer. Chem. Soc.*, 1949, **71**, 286). A solution of the carbinol (8·8 g.) in glacial acetic acid (10 ml.) was stirred at 0° for 6 hours during the dropwise addition of a solution of chromic trioxide (2·5 g.) in water (2·5 ml.) and glacial acetic acid (5 ml.). The reaction mixture was poured on ice (100 g.), and the product isolated with ether. Distillation of the residue left after removal of the dried solvent gave the *ketone* as a colourless mobile liquid (6·0 g., 69%), b. p. 84—86°/0·7 mm., n_D^{25} 1·5309 (Found: C, 66·7; H, 6·7; Cl, 17·9. $C_{11}H_{13}OCl$ requires C, 67·2; H, 6·6; Cl, 18·1%). The *oxime*, prepared in the usual way, crystallised from ethyl alcohol in colourless monoclinic prisms, m. p. 218—219° (Found: C, 63·2; H, 6·6; Cl, 17·0. $C_{11}H_{14}ONCl$ requires C, 62·4; H, 6·6; Cl, 16·8%). The *semicarbazone* crystallised from aqueous ethyl alcohol in monoclinic prisms, m. p. 208—209° (softens at *ca.* 125°) (Found: C, 56·8; H, 6·4; Cl, 13·6. $C_{12}H_{16}ON_3Cl$ requires C, 56·8; H, 6·3; Cl, 14·0%).

1-p-*Chlorophenyl*-1-p-*tolyl*-2 : 2-*dimethylpropan*-1-*ol* (VIII; R = Cl, R′ = Me, R″ = OH).—An ethereal solution of the above ketone (12·9 g.) was added with shaking to an ice-cooled ethereal solution of *p*-tolylmagnesium bromide, prepared from magnesium turnings (2·9 g.) and *p*-bromotoluene (20·5 g.) in ether (50 ml.), and heated under reflux for 4—6 hours. The mixture was cooled in ice and decomposed by 2*N*-sulphuric acid. The ethereal layer, after being washed with water and sodium hydrogen sulphite and saturated sodium hydrogen carbonate solutions, was dried (Na_2SO_4), and the solvent removed. Distillation of the residue gave a fore-run consisting mainly of *p*-bromotoluene, and finally 1-p-*chlorophenyl*-1-p-*tolyl*-2 : 2-*dimethylpropan*-1-*ol* (12·7 g., 67%), b. p. 158—160°/0·7 mm., n_D^{25} 1·5811 (Found: C, 75·3; H, 7·7; Cl, 11·1. $C_{18}H_{21}OCl$ requires C, 74·9; H, 7·3; Cl, 12·3%). Confirmation of the structure was obtained by chromic acid oxidation which gave *p*-chlorophenyl *p*-tolyl ketone, m. p. 126—127°, undepressed by admixture with an authentic specimen.

1-p-*Chlorophenyl*-1-p-*tolyl*-2 : 2-*dimethylpropane* (V; R = Cl, R′ = Me).—This asymmetrical DDT *analogue* was obtained by reduction of the corresponding carbinol (VIII; R = Cl, R′ = Me, R″ = OH) as already described for the symmetrical hydrocarbons (V; R = R′ = Cl or Me). It was isolated as a mobile, water-white liquid (80%), b. p. 138—140°/0·6 mm., n_D^{25} 1·5713 (Found: C, 80·3; H, 7·7; Cl, 12·8. $C_{18}H_{21}Cl$ requires C, 79·3; H, 7·7; Cl, 13·0%).

Di-p-chlorophenylacetyl Chloride.—Di-*p*-chlorophenylacetic acid (42 g.), prepared by the method of Grummitt, Buck, and Egan (*Org. Synth.*, 1946, **26**, 24), was heated under reflux for 3 hours with thionyl chloride (82 g.) which had been freshly distilled after being kept for 18 hours over a little linseed oil. After removal of excess of reagent, the chloride was distilled (41·7 g., 93%); it had b. p. 190°/2 mm. (Found: Cl, 34·6. Calc. for $C_{14}H_9OCl_3$: Cl, 35·5%). Grummitt and Marsh (*J. Amer. Chem. Soc.*, 1949, **71**, 4156) report the isolation of an oily acid chloride which decomposed on attempted distillation at 3—4 mm.; Erlenmeyer *et al.* (*loc. cit.*) give m. p. 57—59°.

Di-p-chlorophenylacetamide.—Reid and Hunter's method (*J. Amer. Chem. Soc.*, 1948, **70**, 3515) for diphenylacetamide was employed. The above acetyl chloride (25·8 g.) was added gradually to ammonia solution (*d* 0·88; 250 ml.) and boiled for 10 minutes with occasional shaking. The product (21·8 g., 90%) crystallised from ethyl alcohol in stout rhombs, m. p. 156—157°. Grummitt and Marsh (*loc. cit.*) give m. p. 152—154°.

Di-p-chlorophenylacetonitrile.—Reid and Hunter's method (*loc. cit.*) was modified as follows. Di-*p*-chlorophenylacetamide (9·3 g.) and redistilled phosphorus oxychloride (2·2 ml.) were heated at 100° for 2 hours, and then poured on crushed ice. The product (8 g., 92%) isolated with ether crystallised from ethyl alcohol in aggregates of hexagonal prisms, m. p. 88—89° (Found: C, 64·3; H, 3·8; Cl, 27·2. Calc. for $C_{14}H_9NCl_2$: C, 64·1; H, 3·4; Cl, 27·1%). Grummitt and Marsh (*loc. cit.*) give m. p. 85—86°.

Di-p-tolylacetic Acid.—1 : 1-Dichloro-2 : 2-di-*p*-tolylethylene (44·4 g.) and powdered potassium hydroxide (27·2 g.) were refluxed for 24 hours in diethylene glycol (350 ml.) and then poured on crushed ice (1 kg.). After extraction of the neutral matter with ether, the solution was acidified with concentrated hydrochloric acid, and the product isolated with ether. Removal of the dried solvent gave the acid (20·4 g., 53%), from which traces of diethylene glycol were removed by boiling with water. Crystallisation from methyl alcohol gave a mass of colourless needles, m. p. 143—144°. Fritsch and Feldmann (*Annalen*, 1899, **306**, 81) give m. p. 144°.

1 : 1-*Di*-p-*chlorophenyl*-2 : 2-*dimethylpropan*-2-*ol* (X; R = R′ = Cl, R″ = OH).—Ethyl di-*p*-chlorophenylacetate (35·2 g.) in absolute ether (50 ml.) was added dropwise to a vigorously stirred ethereal solution of methylmagnesium iodide (from methyl iodide, 17·2 ml., and magnesium turnings, 7·2 g.). After refluxing for 4 hours, the reaction mixture was cooled and decomposed with 2*N*-sulphuric acid, and the product isolated with ether. Distillation of the residue after removal of the solvent gave a viscous liquid (31 g., 92%), b. p. 175—178°/0·4 mm. After being kept at 0° for 24 hours this liquid solidified and crystallised from light petroleum (b. p. 40°) in massive prisms, m. p. 76—77° (Found: C, 65·1; H, 5·5; Cl, 24·0. $C_{16}H_{16}OCl_2$ requires C, 65·1; H, 5·4; Cl, 24·1%). Attempts to acetylate or *p*-nitrobenzoylate this *propanol* and to prepare a phenyl- or α-naphthyl-urethane were not successful.

1 : 1-*Di*-p-*tolyl*-2 : 2-*dimethylpropan*-2-*ol* (X; R = R′ = Me, R″ = OH).—Ethyl di-*p*-tolylacetate (25·4 g.) reacted with methylmagnesium iodide as described above, and the product was isolated similarly after 18 hours' refluxing. It was obtained as a glassy liquid (23 g., 96%), b. p. 139—162°/0·6 mm., which slowly crystallised. The *propanol* crystallised from light petroleum (b. p. 40°) in large colourless prisms, m. p. 78—79° (Found: C, 84·9; H, 9·0. $C_{18}H_{22}O$ requires C, 85·1; H, 8·7%).

2-*Chloro*-1 : 1-*di*-p-*tolyl*-2-*methylpropane* (X; R = R′ = Me, R″ = Cl).—The foregoing carbinol (2·5 g.) was mixed with phosphorus pentachloride (2·2 g.) and kept overnight. The *chloro*-compound, isolated with ether and washed with sodium hydrogen carbonate solution, remained as a colourless

viscous liquid (2·4 g. 89%) after aspiration of the dry solvent (Found, after drying *in vacuo* over P_2O_5: Cl, 10·3. $C_{10}H_{11}Cl$ requires Cl, 13·0%).

1 : 1-*Di*-p-*chlorophenyl*-2-*methylpropan*-1-*ol* (XV; R = Me, R′ = OH).—Ethyl *iso*butyrate (3·8 g.) in anhydrous ether (25 ml.) was added with cooling and shaking to a solution of *p*-chlorophenylmagnesium bromide (from *p*-chlorobromobenzene, 19·2 g., and magnesium, 2·4 g., in anhydrous ether, 100 ml.). After being kept overnight, the mixture was decomposed with 2*N*-sulphuric acid, and the ethereal layer separated and washed with water and sodium hydrogen carbonate, and finally dried (Na_2SO_4). Removal of the solvent and distillation of the residue gave a fraction (2·5 g.), b. p. <80°/0·6 mm., and the tertiary *carbinol* (XV; R = Me, R′ = OH) (8·8 g.), b. p. 175—180°/0·6 mm., which quickly solidified. It crystallised from light petroleum (b. p. 60—80°) in large, colourless, hexagonal plates, m. p. 115—116° (Found: C, 65·2; H, 5·5; Cl, 23·5. $C_{17}H_{19}OCl_3$ requires C, 65·1; H, 5·4; Cl, 24·0%). The di-*p*-chlorophenylmethane structure was confirmed by chromic acid oxidation in glacial acetic acid solution, 4 : 4′-dichlorobenzophenone, m. p. 145—147°, being obtained, undepressed on admixture with an authentic specimen.

2-*Chloro*-1 : 1-*di*-p-*chlorophenyl*-2-*methylpropane* (X; R = R′ = R″ = Cl).—The above carbinol (X; R = R′ = Cl, R″ = OH) (3 g.) was mixed with phosphorus pentachloride (2·7 g., 1 mol.) and kept overnight. The product, after isolation with ether and washing with sodium hydrogen carbonate solution, distilled as a colourless viscous liquid (2·6 g.), b. p. 184—186°/1·2 mm. (Found: Cl, 33·3. $C_{17}H_{17}Cl_3$ requires Cl, 34·0%). Treatment of either the crude product or the distilled sample with phosphorus pentachloride at 140° for 2 hours failed to bring about any decomposition.

1 : 1-*Di*-p-*chlorophenyl*-2-*methylprop*-1-*ene* (XII; R = Me).—(*a*) The chloro-compound (X; R = R′ = R″ = Cl) described above (3·7 g.), dissolved in ethyl alcohol (5 ml.), was refluxed for 2 hours with a solution of sodium hydroxide (0·47 g.) in ethyl alcohol (10 ml.). After removal of excess of solvent, water was added and the product extracted with ether and washed with water, and the extract dried (Na_2SO_4). Removal of the ether and distillation of the residue gave the *ethylene* (XII; R = Me) as a viscous liquid (2·9 g.), b. p. 152—156°/0·3 mm. It crystallised from methyl alcohol in prismatic plates, m. p. 69—70° (Found: C, 69·3; H, 5·0; Cl, 25·0. $C_{16}H_{14}Cl_2$ requires C, 69·4; H, 5·0; Cl, 25·6%).

(*b*) 1 : 1-Di-*p*-chlorophenyl-2-methylpropan-1-ol (XV; R = Me, R′ = OH) (1·0 g.), prepared as already described, was heated with an equal weight of anhydrous potassium hydrogen sulphate at 155—160° for 1 hour. On cooling, the product was isolated by trituration with ether, and after removal of the solvent the residual viscous oil crystallised from methyl alcohol in prisms, m. p. 63—65°, undepressed on admixture with the compound prepared as in (*a*).

Oxidation of the ethylene (XII; R = Me) (0·1 g.) in acetic acid (5 ml.) was carried out by refluxing with chromic acid (0·1 g.) for 1 hour in a stream of carbon dioxide. Acetone 2 : 4-dinitrophenylhydrazone, m. p. 123—124°, and 4 : 4′-dichlorobenzophenone, m. p. 146—147°, both undepressed on admixture with authentic specimens, were obtained from the trap and the residue, respectively.

1 : 1-*Di*-p-*chlorophenyl*-2-*methylprop*-2-*ene* (XIII).—The carbinol (X; R = R′ = Cl, R″ = OH) (3 g.) and phosphorus pentachloride (2·7 g., 1 mol.) were heated at 150° for 1 hour. After cooling, the product was isolated with ether, and the extract washed with saturated sodium hydrogen carbonate solution and dried. Removal of the solvent and distillation of the residue gave a viscous liquid (2·4 g.), b. p. 160—165°/0·4 mm., which gradually solidified. Crystallisation from methyl alcohol gave a product (A), m. p. 121—123°, which on recrystallisation from ethyl alcohol gave 1 : 1-*di*-p-*chlorophenyl*-2-*methylprop*-2-*ene* (XIII), (0·35 g.), m. p. 124—124·5° (Found: C, 69·5; H, 4·6; Cl, 25·3. $C_{16}H_{14}Cl_2$ requires C, 69·4; H, 5·0; Cl, 25·6%). Oxidation with chromic acid, as already described for the isomeric compound (XII; R = Me), yielded formaldehyde 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 150—151°. Evaporation of the mother-liquors from (A) gave a product (0·6 g.), m. p. 64—66°, identical with the ethylene (XII; R = Me). Attempts to convert (XIII) into (XII; R = Me) by heating it at 140° for 18 hours either alone or with sodium ethoxide in a sealed tube were not successful In the former case the material was recovered unchanged, and in the latter a brownish amorphous material was obtained which has not yet been fully investigated.

1 : 2-*Dichloro*-1 : 1-*di*-p-*chlorophenyl*-2-*methylpropane*.—The ethylene, m. p. 69—70° (XII; R = Me) was dissolved in chloroform (5 ml.) and saturated with chlorine at 0°. Next morning, excess of chlorine was removed by aspiration, and the product extracted with ether, washed with sodium hydrogen carbonate solution, and dried. Removal of the solvent and distillation of the residue gave the *dichloro*-compound as a pale yellow viscous liquid, b. p. 155—158°/0·5 mm. (Found: Cl, 38·9. $C_{16}H_{14}Cl_4$ requires Cl, 40·8%).

1 : 1-*Di*-p-*chlorophenyl*-2-*methylpropane* (XV; R = Me, R′ = H).—Reduction of either of the ethylenes (XII; R = Me) or (XIII) in ethyl-alcoholic solution by means of Raney nickel and hydrogen at atmospheric pressure gave the *hydrocarbon* (XV; R = Me, R = H) as a colourless viscous liquid, b. p. 142—146°/0·8 mm., n_D^{18} 1·5881 (Found: C, 68·5; H, 5·5; Cl, 25·6. $C_{16}H_{16}Cl_2$ requires C, 68·8; H, 5·7; Cl, 25·4%). Attempts to reduce 1 : 1-di-*p*-chlorophenyl-2-methylpropan-1-ol (XV; R = Me, R′ = OH) in ethyl-alcoholic solution by amalgamated zinc and dry hydrogen chloride resulted in loss of water and formation of the ethylene (XII; R = Me).

Bis-1 : 1-*di*-p-*chlorophenyl*-2-*methyl*-2-*propyl Ether* (XIV).—The carbinol (X; R = R′ = Cl, R″ = OH) (2·0 g.) and fused potassium hydrogen sulphate (2·0 g.) were heated together at 170—180° for 1 hour. The *product* (1·6 g.) isolated with ether was a colourless viscous liquid, b. p. 138—140°/0·2 mm., n_D^{18} 1·5941 (Found: C, 67·4; H, 5·2; Cl, 24·0. $C_{33}H_{30}OCl_4$ requires C, 67·2; H, 5·2; Cl, 24·8%).

p-*Chlorophenyl* p-*Tolyl Ketone*.—Toluene (125 ml.) and powdered aluminium chloride (10·4 g.) were cooled in ice and vigorously stirred during the dropwise addition of *p*-chlorobenzoyl chloride (13·75 g.),

The mixture was kept for 3 days and then decomposed by addition of ice and 2N-hydrochloric acid. The organic layer was separated, excess of toluene distilled off under reduced pressure, and the residue extracted with ether. After being washed with 2N-hydrochloric acid, water, and 10% sodium hydroxide solution, the extract was dried, and the solvent removed. Distillation of the residue gave the ketone (13·3 g., 73%), b. p. 170—180°/3 mm., which crystallised from ethyl alcohol in nacreous plates, m. p. 126—127°. Cohen (*Rec. Trav. chim.*, 1919, **38**, 117) gives m. p. 118°. The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid–dioxan in small, lustrous, vermilion plates, m. p. 209—210° (Found: C, 58·3; H, 3·8; Cl, 8·5. $C_{22}H_{15}O_4N_4Cl$ requires C, 58·5; H, 3·7; Cl, 8·6%).

Reaction of DDT with Methylmagnesium Iodide.—Methylmagnesium iodide (3 mols.) (from methyl iodide, 10·6 ml., and magnesium, 4·2 g., in absolute ether, 70 ml.) was treated with DDT (20·2 g., 1 mol.) and heated under reflux for 7 hours after being kept overnight. The mixture was acidified with 2N-sulphuric acid, and the products isolated with ether. Removal of the dry solvent and distillation yielded a main fraction (5·0 g.), b. p. 150—160°/0·4 mm. Crystallisation from light petroleum (b. p. 40—60°) gave 1 : 1-dichloro-2 : 2-di-*p*-chlorophenylethane (XV; R = Cl, R′ = H), m. p. 109—110° (Found: C, 52·6; H, 3·1. Calc. for $C_{14}H_{10}Cl_4$: C, 52·5; H, 3·1%) undepressed on admixture with an authentic specimen. 4 : 4′-Dichlorostilbene, m. p. 174—175° (Found: C, 67·3; H, 4·0. Calc. for $C_{14}H_{10}Cl_2$: C, 67·5; H, 4·0%) undepressed by an authentic specimen, was also obtained.

Reaction of 1 : 1 : 1-*Trichloro*-2 : 2-*di*-*p*-*tolylethane with Methylmagnesium Iodide.*—This was carried out as above for DDT. The product (6·1 g.), b. p. 136—142°/0·2 mm., from the DDT analogue (10 g.) crystallised from light petroleum (b. p. 40°) in agglomerates of rhombic prisms, m. p. 81—82° undepressed on admixture with an authentic specimen of 1 : 1-dichloro-2 : 2-di-*p*-tolylethane. Brand (*Ber.*, 1913, **46**, 2941) gives m. p. 80°. No stilbene derivative was isolated.

The authors' thanks are due to Mr. R. F. Batt for the chlorine analyses, to Mr. A. Stringer for the insecticidal testing, and to Dr. H. Martin for his interest in this work. One of them (E. J. S.) thanks the Bristol Education Committee for a Scholarship.

Department of Agriculture and Horticulture,
University of Bristol, Research Station,
Long Ashton, Bristol.

[*Received, May 22nd*, 1950.]

---

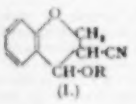
523. *Some Chroman and* 1 : 2-*Benzopyran Derivatives.*

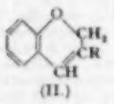
By Helan V. Taylor and Muriel L. Tomlinson.

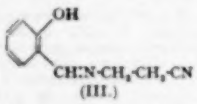
3-Cyanochroman-4-ol and 3-cyano-1 : 2-benzopyran have been prepared by condensation of acrylonitrile with salicylaldehyde in an aqueous alkaline medium. Some derivatives of these substances are described.

We undertook an investigation of the reaction between salicylaldehyde and acrylonitrile as a model experiment to obtain information about the possibility of using acrylonitrile for the preparation of chroman derivatives which might prove useful intermediates for the synthesis of certain naturally occurring substances. Since this work was begun Bachman and Levine (*J. Amer. Chem. Soc.*, 1948, **70**, 599) have published an account of their work on this reaction, and although further work is in progress it seems desirable to publish some of our results at this stage.

Like these authors, we found that there is very little reaction between salicylaldehyde and acrylonitrile when the two substances are heated together with basic catalysts such as sodium or sodium methoxide, and the use of salicylonitrile, which is not chelated like the aldehyde, provided no more promising route to the desired compounds. Nevertheless, assuming that chelation is at any rate one important factor in preventing combination, we investigated the reaction in aqueous alkaline solution and have developed methods by which 3-cyanochroman-4-ol (I; R = H) and 3-cyano-1 : 2-benzopyran (II; R = CN) can be prepared in reasonable


(I.)


(II.)


(III.)

quantities. Bachman and Levine obtained very small yields of these substances, and the m. p. of their substance (I; R = H) was some 11—12° lower than that of our product. (It is of course possible that *cis–trans*-isomerism is responsible for this difference.) We have also isolated a substance which appears to be β-(*o*-hydroxybenzylideneamino)propionitrile (III). This has evidently been formed by condensation of salicylaldehyde with β-aminopropionitrile formed from acrylonitrile and ammonia. An alkaline solution of acrylonitrile smells of ammonia when

warmed; (III) is formed in larger yield if ammonia is added to the reaction mixture and it separates when the solution no longer contains free alkali.

1 : 2-Benzopyran-3-carboxylic acid (II; R = CO_2H) can be obtained by hydrolysis of either (I; R = H) or (II; R = CN), and when (I; R = H) is heated with sodium acetate and acetic anhydride it is converted into a mixture of (II; R = CN) and 4-acetoxy-3-cyanochroman (I; R = Ac). (I; R = H) is not dehydrated by boiling it with phosphoric oxide in benzene or by distilling it *in vacuo*, which may indicate that the 4-OH and the 3-H are *cis* to one another.

Experimental.

3-Cyanochroman-4-ol.—Salicyladehyde (40 g.), acrylonitrile (40 c.c.), and water (30 c.c.) were mechanically stirred and treated, during 5 hours, with sodium hydroxide (12 g.) in water (120 c.c.) as the mixture boiled under reflux. Stirring was continued for a further hour and, on cooling, 3-cyanochroman-4-ol (8·5 g.) separated. It crystallised from alcohol as colourless plates, m. p. 153° (Found: C, 68·9; H, 5·1; N, 8·0. Calc. for $C_{10}H_9O_2N$: C, 69·0; H, 5·1; N, 8·0%). Extraction of the aqueous solution with ether afforded a little more 3-cyanochroman-4-ol, and salicylaldehyde (about 20 g.) was recovered. When kept, the aqueous solution sometimes deposited a small quantity of pale yellow needles, m. p. 74—75°.

β-(o-Hydroxybenzylideneamino)propionitrile.—Salicylaldehyde (12 g.), water (50 c.c.), potassium hydroxide (6 g.), and ammonia (10 c.c.; *d* 0·88) were mixed and slowly treated with acrylonitrile (10 g.) with shaking. After ½ hour, the mixture was heated on a steam-bath for ½ hour, and when it was then kept for several days crystals separated. Recrystallisation from alcohol afforded the *nitrile* as pale yellow needles, m. p. 74—75° (1·0 g.), identical (mixed m. p.) with the compound, m. p. 74—75° (above) (Found: C, 68·9; H, 5·8; N, 16·2. $C_{10}H_{10}ON_2$ requires C, 68·9; H, 5·7; N, 16·1%). This substance dissolves in sodium hydroxide to give a yellow solution and is decomposed by dilute acid with formation of salicylaldehyde (recognised by conversion into the phenylhydrazone). It becomes deep orange on exposure to light but this does not appear to involve appreciable decomposition.

3-Cyano-1 : 2-benzopyran.—Salicylaldehyde (40 g.), acrylonitrile (40 c.c.), and water (100 c.c.) were treated very slowly during 48 hours with sodium hydroxide (6 g.) in water (120 c.c.); the mixture was gently boiled. After a further 24 hours the solution was extracted with ether, and the ether washed with sodium hydroxide and then water. After drying (Na_2SO_4) and evaporation, 3-cyano-1 : 2-benzopyran (10 g.) remained. It crystallised from light petroleum (b. p. 40—60°) as colourless prisms, m. p. 50° (Found: C, 76·3; H, 4·7; N, 8·7. Calc. for $C_{10}H_7ON$: C, 76·4; H, 4·5; N, 8·9%). Bachman and Levine give m. p. 48—49°. Salicylaldehyde (17 g.) was recovered.

1 : 2-*Benzopyran-3-carboxylic Acid.*—3-Cyanochroman-4-ol (or 3-cyano-1 : 2-benzopyran) was refluxed with 10% aqueous sodium hydroxide until evolution of ammonia ceased (about 30 minutes). Acidification then gave a good yield of 1 : 2-*benzopyran-3-carboxylic acid*, which crystallised from alcohol as slightly yellow prisms, m. p. 190° (Found: C, 68·5; H, 4·6. $C_{10}H_8O_3$ requires C, 68·2; H, 4·5%). The *methyl* ester was obtained when this acid or 3-cyanochroman-4-ol was boiled with methyl-alcoholic hydrogen chloride for 1½ hours. It separated from methyl alcohol as colourless plates, m. p. 57° (Found: C, 69·6; H, 5·2. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·2%).

Action of Acetic Anhydride on (I; R = H).—3-Cyanochroman-4-ol (3 g.), sodium acetate (3 g.), and acetic anhydride (15 c.c.) were boiled for 2 hours. On addition of water the product slowly solidified. Recrystallisation from a little alcohol gave 4-*acetoxy*-3-*cyanochroman* (0·9 g.), which was obtained as nearly colourless needles on recrystallisation from light petroleum (b. p. 80—100°) (Found: C, 65·9; H, 5·2. $C_{12}H_{11}O_3N$ requires C, 66·3; H, 5·1%). Addition of water to the alcoholic mother-liquor precipitated an oil which solidified. After drying, this was extracted with cold light petroleum (b. p. 40—60°), and 3-cyano-1 : 2-benzopyran (1·4 g.) was obtained on evaporation. When 4-acetoxy-3-cyanochroman (0·3 g.) was dissolved in a solution containing potassium hydroxide (0·3 g.), alcohol (2 c.c.), and water (2 c.c.), and the solution was kept at room temperature for one hour, 3-cyanochroman-4-ol (identified by mixed m. p.) was obtained on dilution with water.

The Dyson Perrins Laboratory, Oxford University. [*Received, June 15th*, 1950.]

---

524. *The Synthesis of Long-chain Aliphatic Acids from Acetylenic Compounds. Part IV. A New Approach to the Synthesis of Branched-chain Acids.*

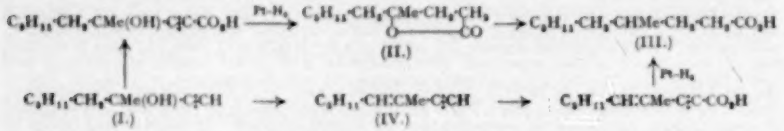
By C. L. Leese and R. A. Raphael.

Good methods of synthesis of monomethyl-substituted long-chain fatty acids are described which employ the easily accessible methyl ketones and readily available acetylenic compounds.

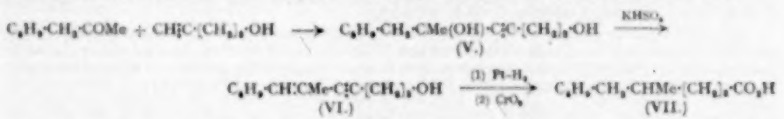
The isolation of the branched-chain fatty acids tuberculostearic acid, phthioic acid, and mycocerosic acid from tubercle bacilli and the investigation of their lesion-producing properties (for review, see Weitzel, *Angew. Chem.*, 1948, **60**, 263) have stimulated considerable study of the synthesis of such methyl-substituted compounds. The methods available for the

preparation of the monomethyl acids fall into two classes, *i.e.*, the repeated homologation by classical procedures of a branched-chain starting material (Polgar and Robinson, *J.*, 1943, **615**; 1945, **389**; 1949, **1545**; Wilson, *J. Amer. Chem. Soc.*, 1945, **67**, 2162; Stenhagen *et al.*, *Svensk Kem. Tids.*, 1942, **54**, 145; *Arkiv Kem. Min. Geol.*, 1946, **22**, *A*, No. 19; 1948, **26**, *A*, No. 12) or the condensation of the relevant branched-chain cadmium dialkyl with an ω-carbethoxyalkanoyl chloride followed by reduction of the keto-ester produced (Cason *et al.*, *J. Amer. Chem. Soc.*, 1942, **64**, 1106; 1944, **66**, 1764; 1947, **69**, 1233; 1948, **70**, 298; *J. Org. Chem.*, 1948, **13**, 227, 239; 1949, **14**, 132, 137, 147, 155; 1950, **15**, 135, 139, 148). The first of these processes is often very tedious, and the disadvantages of the latter have recently been pointed out by Ames, Bowman, and Mason (*J.*, 1950, 174).

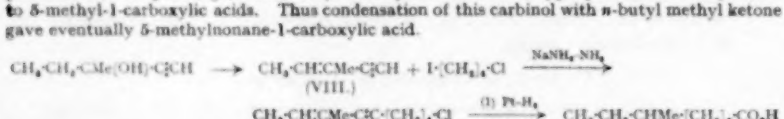
The present interest in acetylenic compounds, resulting in the ready availability of many members of the series, suggested their use for the synthesis of branched-chain acids of this type, and examples of this are described below. In each case the branching methyl group is introduced by means of a methyl ketone reactant at the stage in which the complete carbon skeleton is formed, thus obviating the necessity of preparing a branched-chain intermediate.



The scheme delineates an example of a general method for preparing 3-methyl-1-carboxylic acids. 3-Methylnon-1-yn-3-ol (I; prepared from hexyl methyl ketone and sodium acetylide) was carboxylated by the method of Haynes and Jones (*J.*, 1946, 503), and the resulting acetylenic hydroxy-acid catalytically hydrogenated to the lactone (II). Fission of this lactone by the procedure of Cason *et al.* (1944, *loc. cit.*) furnished the corresponding ethylenic ester which, after hydrogenation and hydrolysis, yielded 3-methylnonane-1-carboxylic acid (III). As the lactone fission did not proceed smoothly, the following variant was adopted with considerable enhancement in the yield of the final acid. Catalytic dehydration of the carbinol (I) over aluminium phosphate (Heilbron, Jones, and Richardson, *J.*, 1949, 287) produced 3-methylnon-3-en-1-yne (IV); carboxylation of the derived Grignard complex and hydrogenation of the unsaturated acid produced gave an excellent yield of the acid (III).



For the preparation of 4-methyl-1-carboxylic acids the easily obtainable but-4-yn-1-ol may be employed. Thus, in the example designated above, condensation of the Grignard complex of this carbinol with *n*-amyl methyl ketone furnished the glycol (V). Dehydration of this compound with potassium hydrogen sulphate involved only the tertiary hydroxyl group thus producing 5-methyldec-5-en-3-yn-1-ol (VI) which, after hydrogenation and oxidation, gave 4-methylnonane-1-carboxylic acid (VII). The use of pent-5-yn-1-ol (obtainable from tetrahydrofurfuryl chloride in excellent yield; Eglinton, Jones, and Whiting, forthcoming publication; cf. Jones, *J.*, 1950, 756) in a synthesis of this type provides a ready route to 5-methyl-1-carboxylic acids. Thus condensation of this carbinol with *n*-butyl methyl ketone gave eventually 5-methylnonane-1-carboxylic acid.



The recently perfected method of preparing long-chain ωω-chloro-iodides (Ahmad and Strong, *J. Amer. Chem. Soc.*, 1948, **70**, 1699, 3391) suggested their condensation with branched-chain vinylacetylenes to provide intermediates of obvious use in this field. The above series of reactions represents an example of this procedure. Dehydration of 3-methylpent-1-yn-3-ol

(prepared from ethyl methyl ketone and sodium acetylide) furnished 3-methylpent-3-en-1-yne (VIII). Condensation of the sodium salt of this hydrocarbon with 1-chloro-4-iodobutane produced the unsaturated chloride (IX); hydrogenation, nitrile formation, and hydrolysis yielded 7-methylnonane-1-carboxylic acid (X). This method is obviously capable of wide variation and applicability, and the ready availability of the starting materials is another advantage. A restricting factor, however, is the solubility of the sodium salt of the intermediate vinylacetylene, *e.g.*, (VIII), in liquid ammonia; this tends to decrease as the length of the carbon chain increases, with consequent deleterious effect on the yield of condensation product. In order to obviate this, the following series of reactions, exemplified by the synthesis of 9-methylheptadecane-1-carboxylic acid, was evolved.

$$C_5H_{11}\cdot CH_2\cdot COMe + CH{\equiv}C\cdot[CH_2]_4\cdot OR \longrightarrow \underset{\text{(XI.)}}{C_5H_{11}\cdot CH_2\cdot CMe(OH)\cdot C{\equiv}C\cdot[CH_2]_4\cdot OR} \xrightarrow{KHSO_4}$$

$$\underset{\text{(XIII.)}}{C_5H_{11}\cdot CH{:}CMe\cdot C{\equiv}C\cdot[CH_2]_4\cdot OR} \xrightarrow{Pt\text{-}H_2} C_5H_{11}\cdot CH_2\cdot CHMe\cdot[CH_2]_7\cdot OR \xrightarrow{\text{(1) HBr, (2) KCN, (3) Hydrolysis.}}$$

$$\underset{\text{(XIV.)}}{C_5H_{11}\cdot CH_2\cdot CHMe\cdot[CH_2]_7\cdot CO_2H} \qquad [R = o\text{-MeO}\cdot C_6H_4\cdot]$$

Reaction of the sodium salt of guaiacol with excess of 1 : 5-dibromopentane gave 1-bromo-5-*o*-methoxyphenoxypentane which furnished the acetylenic ether (XI) on being treated with sodium acetylide in liquid ammonia. Condensation of the Grignard complex of this ether with methyl nonyl ketone gave the glycol ether (XII) which was readily dehydrated to the unsaturated ether (XIII). Obvious procedures of hydrogenation, ether fission, nitrile formation, and hydrolysis then yielded the final product, 9-methylheptadecane-1-carboxylic acid (XIV). [Guaiacol was used as a protecting agent because of the relative ease of fission of methoxylated phenyl ethers (Ziegler *et al.*, *Ber.*, **1937**, **70**, 1275; **1942**, **75**, 1715).]

Although all the above reactions exemplify the synthesis of compounds with a branching methyl group, they are obviously capable of extension to prepare compounds with a branching group of any size by employing the requisite ketone.

Experimental.

3-Methylnon-1-yn-3-ol.—The reaction of hexyl methyl ketone (256 g.) with sodium acetylide (from sodium, 46 g.) employing the usual procedure gave the acetylenic carbinol (232 g., 76%), b. p. 88°/15 mm., n_D^{20} 1·4409 (Petrov and Harlic, *J. Gen. Chem. Russia*, 1941, **11**, 1100, give b. p. 69°/2 mm.).

3-Methylnon-1-yn-3-ol-1-carboxylic Acid.—The Grignard complex prepared from the above carbinol (77 g.) and ethylmagnesium bromide (from Mg, 29 g.) was treated with excess of solid carbon dioxide in an autoclave by the method of Haynes and Jones (*loc. cit.*). Working up in the usual manner gave the *acid* (80 g., 80%), crystallising from benzene–light petroleum (b. p. 60—80°) in plates, m. p. 76°; a small sample was purified for analysis by high-vacuum sublimation (Found: C, 67·0; H, 9·35. $C_{11}H_{18}O_2$ requires C, 66·65; H, 9·15%). The *S-benzylisothiuronium* salt crystallised from aqueous alcohol in needles, m. p. 162° (Found: N, 7·95. $C_{19}H_{28}O_2N_2S$ requires N, 7·95%).

Lactone of 3-Methylnonan-3-ol-1-carboxylic Acid (II).—A solution of the above acetylenic hydroxy-acid (20 g.) in ethyl acetate (50 c.c.) was hydrogenated by use of platinic oxide as catalyst. Removal of catalyst and solvent gave an oil (18 g.), b. p. 112°/0·5 mm., n_D^{20} 1·4487 (Franck *et al.*, *J. Amer. Chem. Soc.*, 1944, **66**, 4, give b. p. 120—125°/4—5 mm. and n_D^{20} 1·4487 for this lactone).

3-Methylnon-3-en-1-yne (IV).—3-Methylnon-1-yn-3-ol (50 g.) was slowly distilled through porous-tile chips coated with aluminium phosphate at 300°/25 mm. in a nitrogen atmosphere; the operation was complete in 2 hours. The wet distillate was diluted with ether, and the solution dried ($MgSO_4$); evaporation of the solvent and distillation gave the *nonenyne* (IV) (32 g.) as a colourless, mobile liquid, b. p. 53°/11 mm., n_D^{20} 1·4464 (Found: C, 88·5; H, 12·2. $C_{10}H_{18}$ requires C, 88·15; H, 11·85%). Light absorption in ethanol: Maximum, 2240 A.; ε = 11,000.

3-Methylnon-3-en-1-yne-1-carboxylic Acid.—The hydrocarbon (IV) (25 g.) in an equal volume of dry benzene was added to a benzene solution of ethylmagnesium bromide (from Mg, 4·85 g.), and the stirred mixture heated by steam under nitrogen for 1 hour. The cooled Grignard complex solution was poured on excess of solid carbon dioxide in an autoclave, which was then sealed and kept for 16 hours at room temperature. Working up in the usual manner gave the *acid* as an unstable, pale yellow oil, b. p. 118°/0·05 mm., n_D^{20} 1·4901 (19 g., 58%) (Found: C, 73·1; H, 8·9. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·95%). Light absorption in ethanol: Maximum, 2420 A., ε = 8500. Inflection, 2710 A., ε = 8000. The *S-benzylisothiuronium* salt was stable and crystallised from aqueous alcohol in needles, m. p. 148° (Found: N, 8·2. $C_{19}H_{26}O_2N_2S$ requires N, 8·1%).

3-Methylnonane-1-carboxylic Acid.—(*a*) The lactone (II) (12·4 g.), thionyl chloride (24 g.), and dry benzene (15 c.c.) were heated under reflux for 3 hours, and then cooled; saturated ethanolic hydrogen chloride (50 c.c.) was added dropwise during 15 minutes, and the mixture heated under reflux for a further 15 minutes. The solvents were then removed under vacuum, and the residue heated under

reflux for 3 hours; hydrogen chloride was steadily evolved. The product on being distilled gave *ethyl 3-methylnon-3-ene-1-carboxylate* (9·4 g.), b. p. 129°/15 mm., n_D^{20} 1·4379 (Found: C, 73·1; H, 11·7. $C_{13}H_{24}O_2$ requires C, 73·55; H, 11·4%). The ester was immediately dissolved in methanol (50 c.c.) and shaken with hydrogen in the presence of platinic oxide. When absorption was complete the catalyst was filtered off, and methanolic potash (30%; 20 c.c.) added. The mixture was heated under reflux for 30 minutes, and the solvent then removed under vacuum; the residue was dissolved in water and the non-saponified matter extracted with ether. Acidification of the aqueous phase with hydrochloric acid and isolation by means of ether furnished the required acid (III) (7 g.), b. p. 152—153°/10 mm., n_D^{20} 1·4395 (Polgar and Robinson, *J.*, 1945, 390, give b. p. 150—151°/10 mm., n_D^{14} 1·4403). The *p*-bromophenacyl ester, m. p. 46°, and the tribromoanilide, m. p. 96°, were prepared by the usual procedures (Polgar and Robinson, *loc. cit.*, give m. p.s 42° and 89·5°; Wilson, *J. Amer. Chem. Soc.*, 1945, **67**, 2162, gives m. p.s 45—46° and 96—97°. These two references will henceforth be designated as P. and W., respectively).

An attempt was made to obtain (III) from the lactone directly by high-pressure hydrogenolysis of the aqueous sodium salt in the presence of copper chromite (Johnson, Goldman, and Schneider, *J. Amer. Chem. Soc.*, 1945, **67**, 1357) but the lactone was reovered unchanged.

(*b*) **3-Methylnon-3-en-1-yne-1-carboxylic acid** (6 g.) in methanol (20 c.c.) was catalytically hydrogenated by means of platinic oxide. When uptake was complete, removal of catalyst and solvent followed by distillation yielded the saturated acid (5·4 g.), b. p. 152°/11 mm., n_D^{20} 1·4400, giving derivatives identical with those described above.

But-4-yn-1-ol.—This carbinol was prepared in 46% yield from ethylene oxide and sodium acetylide in liquid ammonia (cf. Froning and Hennion, *J. Amer. Chem. Soc.*, 1940, **62**, 653). In addition, a high-boiling by-product (7%) was obtained, b. p. 80°/11 mm., n_D^{20} 1·4650 (Found: C, 62·6; H, 8·9. $C_8H_{16}O_3$ requires C, 63·1; H, 8·85%); the compound exhibited alcoholic properties and gave a silver salt and was probably **4-2′-*hydroxyethoxybut*-1-*yne***, $CH{\equiv}C{\cdot}[CH_2]_2{\cdot}O{\cdot}[CH_2]_2{\cdot}OH$.

5-*Methyldeca*-3-*yne*-1 : 5-*diol* (V).—But-4-yn-1-ol (20 g.) was slowly added to a solution of ethylmagnesium bromide (from Mg, 15·2 g.) in ether (500 c.c.), and the stirred mixture heated under reflux in nitrogen for 1 hour. A solution of *n*-amyl methyl ketone (28 g.) in benzene (50 c.c.) was then added dropwise, and the whole heated and stirred under reflux for 36 hours. The complex was decomposed with ice and dilute sulphuric acid, and the product isolated by means of ether in the usual manner. Distillation yielded the *diol* (39 g.) as a viscous colourless oil, b. p. 120—122°/10^{-4} mm., n_D^{20} 1·4725 (Found: C, 71·75; H, 10·6. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·9%).

5-*Methyldec*-5-*en*-3-*yn*-1-*ol* (VI).—A mixture of the diol (V) (12 g.) and fused powdered potassium hydrogen sulphate (3 g.) was distilled at atmospheric pressure; the product distilled between 245° and 260°. It was dissolved in ether (30 c.c.), washed with sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation and distillation gave the unsaturated *carbinol* (10 g.), b. p. 128—129°/12 mm., n_D^{20} 1·4800 (Found: C, 78·95; H, 11·05. $C_{11}H_{18}O$ requires C, 79·5; H, 10·9%). Light absorption in ethanol: Maximum, 2270 A.; ε = 13,000.

5-*Methyldecan*-1-*ol*.—The unsaturated carbinol (VI) (13 g.), dissolved in ethyl acetate (50 c.c.), was catalytically hydrogenated in the presence of platinic oxide. Removal of catalyst and solvent and distillation furnished the saturated *alcohol* (11 g.), b. p. 120—122°/12 mm., n_D^{20} 1·4383 (Found: C, 76·55; H, 14·05. $C_{11}H_{24}O$ requires C, 76·7; H, 14·05%).

4-*Methylnonane*-1-*carboxylic Acid* (VII).—To a stirred solution of 5-methyldecan-1-ol (7 g.) in acetone (30 c.c.) was added slowly a solution of chromium trioxide in sulphuric acid (6N.; 40 c.c.), and stirring was continued at room temperature for 1 hour. Isolation by means of ether gave the acid (VII) (5·5 g.), b. p. 166°/18 mm., n_D^{20} 1·4416 (*p*-bromophenacyl ester, m. p. 49°; tribromoanilide, m. p. 95°) (P. give b. p. 167—168°/20 mm., n_D^{25} 1·4418; m. p.s 50° and 95·5° respectively).

6-*Methyldec*-4-*yne*-1 : 6-*diol*.—To a solution of the Grignard complex derived from pent-4-yn-1-ol (19·6 g.) and ethylmagnesium bromide (from Mg, 13·2 g.) was added a solution of *n*-butyl methyl ketone (23 g.) in benzene (50 c.c.) in a manner analogous to the cognate preparation described above. Isolation in the usual fashion gave **6-*methyldec*-4-*yne*-1 : 6-*diol*** (30 g.) as a viscous, pale yellow oil, b. p. 116°/10^{-4} mm., n_D^{20} 1·4778 (Found: C, 72·2; H, 11·1. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·9%).

6-*Methyldec*-6-*en*-4-*yn*-1-*ol*.—A mixture of the above diol (10 g.) and potassium hydrogen sulphate (3 g.) was distilled under atmospheric pressure and the distillate collecting between 200° and 230° was diluted with ether (30 c.c.), washed with sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation and distillation gave the primary *alcohol* (7 g.), b. p. 79—82°/10^{-4} mm., n_D^{20} 1·4867 (Found: C, 79·3; H, 11·0. $C_{11}H_{18}O$ requires C, 79·5; H, 10·9%). Light absorption: Maximum, 2280 A.; ε = 15,000.

5-*Methylnonane*-1-*carboxylic Acid*.—A solution of the unsaturated carbinol (4 g.) in acetone (20 c.c.) was hydrogenated, platinic oxide being used as catalyst. After removal of the catalyst, the filtrate was treated with a solution of chromium trioxide in sulphuric acid (6N.; 22 c.c.), and the mixture warmed for 30 minutes by steam. The product was extracted with ether, from which the acidic fraction was removed by shaking with sodium hydrogen carbonate solution. Acidification and isolation by means of ether furnished the required acid (2·2 g.), b. p. 155°/12 mm., n_D^{20} 1·4406; *p*-bromophenacyl ester, m. p. 50° (P. give b. p. 164—165°/18 mm., n_D^{20} 1·4403, m. p. 51°).

3-*Methylpent*-3-*en*-1-*yne* (VIII).—3-Methylpent-1-yn-3-ol (70 g.) was slowly distilled in a stream of nitrogen through a tube containing aluminium phosphate-coated porous pot heated to 300°. Drying ($MgSO_4$) and distillation of the product yielded the hydrocarbon (22 g.), b. p. 67—70°, n_D^{20} 1·4318, and unchanged carbinol (27 g.).

1-*Chloro*-7-*methylnon*-7-*en*-5-*yne* (IX).—The hydrocarbon (VIII) (22 g.) in dry ether (50 c.c.) was added to a solution of sodamide (from Na, 11 g.) in liquid ammonia (500 c.c.), and the mixture stirred for one hour. 1-Chloro-4-iodobutane (60 g.; Ahmad and Strong, *loc. cit.*) in dry ether (100 c.c.) was then added, and the stirring continued for 24 hours with constant cooling (carbon dioxide–acetone). The reaction mixture was treated with ammonium chloride (25 g.), and the ammonia allowed to evaporate. Isolation by means of ether in the usual fashion furnished the unsaturated *chloride* (IX) (26 g.) as a pale yellow oil, b. p. 122°/20 mm., n_D^{20} 1·4882 (Found: C, 70·8; H, 9·0. $C_{10}H_{15}Cl$ requires C, 70·4; H, 8·85%). Light absorption in ethanol: Maximum, 2250 A.; $\varepsilon = 9000$.

1-*Chloro*-7-*methylnonane*.—A solution of the unsaturated chloride (IX; 23 g.) in methyl acetate (50 c.c.) was shaken with hydrogen in the presence of platinic oxide until absorption was complete. Removal of catalyst and solvent, followed by distillation, yielded the saturated *chloride* (21 g.), b. p. 113°/20 mm., n_D^{20} 1·4470 (Found: C, 67·7; H, 11·4. $C_{10}H_{21}Cl$ requires C, 67·95; H, 12·0%). The *thiuronium picrate*, prepared by the method of Brown and Campbell (*J.*, 1937, 1699), crystallised from alcohol in yellow needles, m. p. >300°, which detonated violently on rapid heating (Found: N, 15·4. $C_{17}H_{25}O_7N_5S$ requires N, 15·7%).

7-*Methylnonane*-1-*carboxylic Acid*.—The above saturated chloride (14 g.) was heated under reflux with a solution of sodium iodide (25 g.) in dry acetone (200 c.c.) for 12 hours. The precipitated sodium chloride was filtered off, and the solution evaporated; the residue was heated under reflux for 36 hours with a solution of potassium cyanide (9 g.) in aqueous alcohol (80%; 50 c.c.). A solution of potassium hydroxide (9 g.) in water (10 c.c.) was then added, and the mixture heated under reflux for a further 14 hours. Most of the alcohol was removed, and the residue diluted with water and extracted with ether to remove non-acidic material. The aqueous layer was acidified, and the precipitated oil isolated by means of ether. Distillation furnished 7-*methylnonane*-1-*carboxylic acid* (X) (9·2 g.), b. p. 175°/25 mm., n_D^{20} 1·4460 (Found: C, 70·6; H, 11·7. $C_{11}H_{22}O_2$ requires C, 70·9; H, 11·9%). The *p-bromophenacyl* ester crystallised in plates, m. p. 49°, from alcohol (Found: C, 58·9; H, 7·0. $C_{19}H_{27}O_3Br$ requires C, 59·5; H, 7·1%). Evaporation of the ethereal solution of unhydrolysed material yielded the *amide* (1·4 g.), crystallising from alcohol in plates, m. p. 82° (Found: C, 71·05; H, 12·15; N, 7·85. $C_{11}H_{23}ON$ requires C, 71·3; H, 12·5; N, 7·55%).

1-*Bromo*-5-*o*-*methoxyphenoxypentane* (first prepared by A. W. Nineham).—To a solution of sodium (11·5 g.) in absolute alcohol (250 c.c.) was added guaiacol (63 g.) in alcohol (50 c.c.), and the mixture heated by steam for 30 minutes. 1 : 5-Dibromopentane (460 g., 4 mols.) was then rapidly added, and the heating continued for 16 hours. Dilution with an equal volume of water, isolation by means of ether, and distillation furnished 1 : 5-dibromopentane (308 g.) and then 1-*bromo*-5-*o*-*methoxyphenoxypentane* (103 g.), b. p. 145—147°/1 mm. (Found: Br, 28·9. $C_{12}H_{17}O_2Br$ requires Br, 29·3%).

1-*o*-*Methoxyphenoxyhept*-6-*yne* (XI) (first prepared by A. W. Nineham).—The above bromo-ether (75 g.) in dry ether (50 c.c.) was slowly added to a stirred solution of sodium acetylide (from Na, 14·2 g.) in liquid ammonia (1 l.), and stirring continued for 3 hours. Ammonium chloride (25 g.) was then added, the ammonia allowed to evaporate, and the product isolated by means of ether in the usual fashion. Distillation gave 1-*o*-*methoxyphenoxyhept*-6-*yne* (55 g.) as a viscous oil, b. p. 122°/10^{-3} mm., which solidified, when kept, to a crystalline mass of needles, m. p. 41° (Found: C, 76·8; H, 8·4. $C_{14}H_{18}O_2$ requires C, 77·05; H, 8·3%).

1-*o*-*Methoxyphenoxy*-8-*methylheptadec*-6-*yn*-8-*ol* (XII).—To the solution obtained by heating under reflux for 2 hours the foregoing compound (XI) (95 g.) and ethylmagnesium bromide (from Mg, 14·5 g.) in ether (750 c.c.) was added methyl *n*-nonyl ketone (90 g.) in benzene (100 c.c.), and the mixture was heated under reflux for 36 hours. Decomposition with saturated ammonium chloride solution and isolation in the usual manner gave the acetylenic *carbinol* (XII) (112 g.), b. p. 218°/10^{-3} mm., n_D^{20} 1·5038, as a viscous oil which solidified on being cooled to 0° (Found: C, 77·6; H, 10·6. $C_{25}H_{40}O_3$ requires C, 77·3; H, 10·4%).

1-*o*-*Methoxyphenoxy*-8-*methylheptadec*-8-*en*-6-*yne* (XIII).—A mixture of the acetylenic carbinol (XII) (50 g.) and fused powdered potassium hydrogen sulphate (10 g.) was heated at 0·5 mm. pressure. Water was vigorously evolved when the bath-temperature reached 200°, and the product distilled between 215° and 220°. The product was diluted with ether, washed with sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation and distillation furnished the unsaturated ether (XIII) (34 g.), b. p. 186°/10^{-3} mm., n_D^{20} 1·5100 (Found: C, 80·8; H, 10·4. $C_{25}H_{38}O_2$ requires C, 81·05; H, 10·35%). Light absorption in ethanol: Maximum, 2260 A.; $\varepsilon = 25{,}000$.

1-*o*-*Methoxyphenoxy*-8-*methylheptadecane*.—The above ether (XIII) (9 g.) in ethyl acetate (20 c.c.) was shaken with hydrogen in the presence of platinic oxide. When absorption was complete, removal of catalyst and solvent followed by distillation gave the *heptadecane* (8 g.), b. p. 178°/10^{-3} mm., n_D^{20} 1·4878 (Found: C, 79·3; H, 11·95. $C_{25}H_{44}O_2$ requires C, 79·7; H, 11·8%).

1-*Bromo*-8-*methylheptadecane*.—To a solution of the above saturated ether (40 g.) in acetic anhydride (100 c.c.) was slowly added hydrobromic acid (48%; 200 c.c.), and the mixture heated under reflux for 72 hours. The product was cooled, diluted with an equal volume of water, and continuously extracted with light petroleum (b. p. 40—60°). The extract was washed with 2N-sodium hydroxide and dried ($MgSO_4$); evaporation and distillation gave 1-*bromo*-8-*methylheptadecane* (26 g.), b. p. 134°/10^{-3} mm., n_D^{20} 1·4630 (Found: C, 64·8; H, 11·15. $C_{18}H_{37}Br$ requires C, 64·85; H, 11·2%). The *thiuronium picrate*, prepared in the usual manner, crystallised from alcohol in needles, m. p. 111° (Found: N, 12·35. $C_{25}H_{41}O_7N_5S$ requires N, 12·55%).

8-*Methylheptadecane*-1-*carboxylic Acid* (XIV).—A mixture of 1-bromo-8-methylheptadecane (13 g.), potassium cyanide (6 g.), and aqueous alcohol (80%; 50 c.c.) was heated under reflux for 48 hours. Potassium hydroxide (6 g.) in water (10 c.c.) was added, and the solution heated under reflux for a further 36 hours. It was then diluted with an equal volume of water, and the unhydrolysed material

extracted with ether; acidification of the aqueous layer with concentrated hydrochloric acid followed by isolation by means of ether yielded 8-methylheptadecane-1-carboxylic acid (XIV) (11 g.), b. p. 168°/10^{-3} mm., n_D^{25} 1·4530, which soon solidified and crystallised from acetone in prismatic plates, m. p. 40—41° (Found: C, 76·9; H, 12·9. Calc. for $C_{19}H_{38}O_2$: C, 76·5; H, 12·85%). The amide prepared by way of the acid chloride formed plates, m. p. 70°, from alcohol (Found: N, 4·9. Calc. for $C_{19}H_{39}ON$: N, 4·7%); the tribromoanilide, m. p. 90°, crystallised from alcohol in plates (Found: N, 2·3. Calc. for $C_{31}H_{46}ONBr_3$: N, 2·3%) (Cason and Winans, *J. Org. Chem.*, 1950, **15**, 139, give m. p. 38·5—39·1° for the acid, m. p. 69·8—70·5° for the amide, and m. p. 90—91·6° for the tribromoanilide).

The authors thank Sir Ian Heilbron, D.S.O., F.R.S., for his interest in this work which was carried out during the tenure of an I.C.I. Fellowship (R. A. R.), a Senior County Award of the London County Council (C. L. L.), and a Chemical Society Research Grant. The light-absorption data were kindly determined by Dr. E. A. Braude.

Imperial College of Science and Technology,
S. Kensington, London, S.W.7. [*Received, June 17th*, 1950.]

---

525. *A Theoretical Treatment of the Diels–Alder Reaction. Part II. Polyenes, Arylpolyenes, and Related Molecules.*

By R. D. Brown.

The reactivities towards maleic anhydride of the linear polyenes, phenylpolyenes, and various arylpolyenes are discussed in terms of the localisation theory of organic reactions, the para-localisation energies, introduced in Part I (*J.*, 1950, 691), being again used as the appropriate localisation quantities. It is shown that the theory gives an adequate interpretation of the Diels–Alder properties of these molecules when the steric factors involved are taken into account. The latter are shown to introduce some uncertainty into the making of predictions of reactivities for some molecules, and a possible method of overcoming this is mentioned.

In Part I (*J.*, 1950, 691) the reactivities towards maleic anhydride of various polycyclic aromatic hydrocarbons were discussed, and it was shown that these could be explained semiquantitatively in terms of quantities termed para-localisation energies, these being computed by the L.C.A.O. molecular orbital approximation. In the present paper polyenes, arylpolyenes, and related molecules are studied by the same method.

The application of the localisation theory to molecules of the polyene and arylpolyene type involves additional assumptions which are not required in the case of polycyclic hydrocarbons. For instance, in the latter the carbon atoms comprising the conjugated system are all coplanar, but in the case of polyenes and derivatives this is not necessarily so, rotation about carbon–carbon bonds of low mobile order being possible. In addition, with molecules of the butadiene type, carbon atoms 1 and 4 can take up two possible positions of minimum energy, only one of these, the boat configuration, being sterically favourable for a diene addition. Hence, during the following discussion it must be borne in mind that the para-localisation energies have all been computed on the assumption that the conjugated systems involved are entirely coplanar, and in discussing the relative reactivities of pairs of positions it is assumed that the latter are always orientated in the boat configuration. In those cases where either boat or chair configurations are possible and neither is favoured by other steric considerations the relative rates, k_s [as in Part I (*loc. cit.*) these represent approximations to the rates of reaction relative to anthracene ($P' = -2{\cdot}07\gamma$); more specifically $k_s = \exp. 56{\cdot}7(2{\cdot}07 - p'/\gamma)$], should be multiplied by a frequency factor expressing the probability for the molecule possessing the boat configuration, and conversely for $k_b = \exp. 56{\cdot}7(1{\cdot}77 - P'/\gamma)$ (k_b similarly represents the rate relative to that of butadiene). However, it is unlikely that the theoretical rates could give more than orders of magnitude, so this factor will be sufficiently close to unity to be neglected unless steric interactions make the boat configuration very improbable. Some such cases are discussed below.

The para-localisation energies of various pairs of positions for the linear polyenes are listed in Table I. These indicate that the reactivity decreases with increasing chain length, and also that addition to the end of the chain is preferred. Both of these generalisations are in contrast to those for the polyacenes (Part I). However, except in the case of butadiene, addition to the end of the chain (1 : 4 addition) leaves a residual molecule for which N, the number of separate conjugated systems comprising the residual molecule, is 2, whereas addition further along the chain leaves a residual molecule with $N = 3$. As pointed out in Part I, for a given value of

P or P', when N is 3 the molecule will be more reactive than when N is 2, so the question arises whether this effect is great enough to reverse the relative reactivities as indicated simply by P or P'. Addition to the polyene $C_{2n}H_{2n+2}$ leaves a residual molecule (r.m.) comprised of the polyene $C_{2n-4}H_{2n-3}$ and ethylene ($N = 2$) in the case of 1 : 4-addition. 2 : 5-Addition leaves as r.m. two radicals and ethylene, this likewise applying to addition to positions $2r : 2r + 3$ generally. Addition to any of these positions is ruled out by the relatively great instability of radicals. Addition to positions $2r + 1 : 2r + 4$ gives as r.m. the polyenes $C_{2r}H_{2r+2}$, $C_{2n-2r-4}H_{2n-2r-3}$, and ethylene, these together being less stable than the r.m. corresponding to

TABLE I.

The linear polyenes.

Molecule.	Position.	N.	P ($-\beta$).	P'. ($-\gamma$).	P'. kcals.*	k_a.
Butadiene	1 : 4	1	2·47	1·77	69	2×10^7
Hexatriene	1 : 4	2	2·99	1·99	68	90
	2 : 5	3	4·99	3·59	122	—
Octatetraene	1 : 4	2	3·05	2·04	69	5
	2 : 5	3	4·69	3·32	113	—
	3 : 6	3	3·52	2·21	75	—
Decapentaene	1 : 4	2	3·07	2·06	70	2
	2 : 5	3	4·59	3·23	110	—
	3 : 6	3	3·58	2·27	77	1×10^{-4}
	4 : 7	3	4·41	3·06	104	—
Infinite polyene	1 : 4	2	3·093	2·083	71	0·5
	2 : 5	3	4·336	3·004	102	—
	3 : 6	3	3·639	2·325	79	—
	4 : 7	3	4·082	2·756	94	—
	5 : 8	3	3·714	2·392	81	—

* The conversion factor used was $\gamma = -34$ kcals. mole^{-1} as in Part I (*loc. cit.*).

TABLE II.

*Arylethylenes.**

Ethylene.	Position.	N.	P ($-\beta$).	P'. ($-\gamma$).	P'. kcals.	k_a.
Phenyl	2 : 2′	1	3·44	2·42	82	10^{-6}
1 : 2-Diphenyl	2 : 2′	2	3·89	2·60	88	10^{-12}
1 : 1-Diphenyl	2 : 2′	1	3·34	2·35	80	10^{-7}
1 : 1 : 2-Triphenyl	1 : 2‴	3	4·32	2·73	93	—
	2 : 2′	2	3·84	2·54	86	—
1′-Naphthyl	2 : 2′	1	3·26	2·22	75	10^{-4}
2′-Naphthyl	2 : 1′	1	3·17	2·19	74	10^{-5}
	2 : 3′*	1	4·2-*c*	2·8-*c*′	—	—
1′-Anthryl	2 : 2′	1	3·21	2·21	75	10^{-4}
	9′ : 10′	2	3·34	2·10	71	0·2
2′-Anthryl	2 : 1′	1	3·12	2·14	73	0·02
	9′ : 10′	2	3·32	2·08	71	0·6
	2 : 3′*	1	4·2-*c*	2·9-*c*′	—	—
9′-Anthryl	2 : 1′*	1	4·6-*c*	—	—	—
	9′ : 10′	3	3·79	2·26	77	2×10^{-6}
1′-Phenanthryl	2 : 2′	1	3·31 †	2·30 †	78	10^{-6}
2′-Phenanthryl	2 : 1′	1	3·23	2·25	76	10^{-6}
3′-Phenanthryl	2 : 2′*	1	4·1-*c*	—	—	—
	2 : 4′	1	3·25	2·27	77	10^{-6}
4′-Phenanthryl	2 : 3′	1	3·31 †	2·29 †	78	10^{-6}
9′-Phenanthryl	2 : 10′	1	3·07	2·09	71	0·3

* c and c' refer to conjugation energies in units of $-\beta$ and $-\gamma$, respectively. Their magnitudes are generally of the order of 0·4 and 0·2, respectively, and in the table they refer to conjugation energies for :

a, ethylene + *o*-benzoquinodimethane
b, ethylene + 2 : 3-naphthaquinodimethane
c, ethylene + 1 : 3-naphthaquinodimethane
d, ethylene + 1 : 2-naphthaquinodimethane

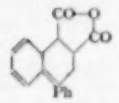
† The resonance energies of the residual molecules were computed by using the annelation energy equations (Brown, *Trans. Faraday Soc.*, in the press).

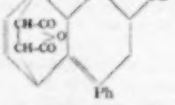
1 : 4-addition by the direct conjugation energy of the two polyenes. The para-localisation energies are computed by assuming each conjugated system in the r.m. to be quite separate in the activated complex, but the latter will always be further stabilised by indirect conjugation through the (not completely) localised carbon atoms involved in the addition. For 1 : 4-addition the neglected stabilisation of the r.m. is from the indirect conjugation energy of the two systems through the localised carbon atom 4, whereas for $2r + 1 : 2r + 4$ addition it is derived from the indirect conjugation energy of the three parts through both localised atoms. These indirect conjugation energies must necessarily be considerably smaller than the direct conjugation energy, especially as the two carbon atoms will now be approaching sp^3 hybridisation, so we may conclude that the secondary effects due to difference in the value of N for 1 : 4- and $2r + 1 : 2r + 4$-additions are not nearly sufficient to reverse the relative reactivities deduced simply from the respective values of P or P'.

These results are in excellent agreement with the scanty experimental data—hexatriene undergoes 1 : 4-addition with maleic anhydride (Kharasch and Sternfeld, *J. Amer. Chem. Soc.*, 1939, **61**, 2318; Kharasch, Nudenberg, and Sternfeld, *ibid.*, 1940, **62**, 2034), and the observation that octatetraene gives only a di-adduct (Woods and Schwartzman, *ibid.*, 1949, **71**, 1396) confirms that butadiene (the conjugated system present in the mono-adduct) is more reactive than octatetraene. It also indicates that addition to the end of the octatetraene chain is preferred.

Table II gives the para-localisation energies for various possible reactive positions (other less reactive positions being eliminated by using the principle, enunciated in Part I, that only pairs of positions giving rise to relatively stable r.m. will be reactive) for a number of arylethylenes. Considering, first, the phenylethylenes, these are known to be unreactive except 1 : 1-diphenylethylene (Bergmann and Bergmann, *ibid.*, 1937, **59**, 1443; Wagner-Jauregg, *Ber.*, 1930, **63**, 3213) for which the primary addition appears to be 2 : 2', in good agreement with the position predicted by the data in Table II. This mono-adduct (I) contains a conjugated system equivalent to 1-phenylhexatriene fixed in a position sterically favourable for 3 : 6-

(I.)





(II.)

addition. As seen from Table VI, these are the most reactive positions for hexatriene and considerably more reactive than the original diphenylethylene, so the second addition should occur very rapidly to give the di-adduct (II). In agreement with this, Wagner-Jauregg (*loc. cit.*; *Annalen*, 1931, **491**, 1) could only isolate the di-adduct but questioned the structure for the latter on the grounds that it behaved as saturated towards reagents such as perbenzoic acid, but it is difficult to formulate an unreactive product by any type of addition of one mole of maleic anhydride to (I).

The values of P' listed for the phenylethylenes are in good accord with the experimentally observed reactivities, the critical range for reactivity, in Part I fixed as between $-2{\cdot}26\beta$ and $-2{\cdot}40\beta$ (values for reactive 1 : 2·5 : 6-dibenzanthracene and unreactive naphthalene, respectively) being in fair agreement with the observation (Wagner-Jauregg, *loc. cit.*) that 1 : 1-diphenylethylene ($P' = -2{\cdot}35\beta$) requires long heating to afford a satisfactory reaction. The values of P for these compounds indicate, however, that styrene ($P = -3{\cdot}44\beta$) should also be reactive (corresponding critical range for P : $-3{\cdot}51\beta$ to $-3{\cdot}68\beta$) and it does not seem possible to attribute this discrepancy to the increased amount of (neglected) indirect conjugation energy due to N having the value 1 for styrene and 2 for the compounds from which the critical range was determined. Thus it appears that P' is more reliable as a criterion of reactivity for arylpolyenes than P. The same point arises in connection with the vinylanthracenes (see below); a possible explanation for this failure will be advanced later.

The data for 1- and 2-vinylnaphthalene predict that both should add maleic anhydride, the 2-isomer being slightly more reactive. Cohen and Warren's experimental results (*J.*, 1937, 1315) confirm the reactivities; the observation of Arbuzov, Salmina, and Sharpshinskaya (*Trans. Butlerov Inst. Chem. Tech. Kazan*, 1934, No. 2, 9; *Chem. Abs.*, 1935, **29**, 3672) is presumably unreliable, the reactivity of 1-vinylnaphthalene being confirmed by Bergmann and

Bergmann (*loc. cit.*). The respective reaction conditions employed indicate that both are more reactive than 1 : 1-diphenylethylene, in good agreement with the theoretical results.

The para-localisation energy for vinylanthracenes point to 9 : 10-addition in all cases, and somewhat less readily than anthracene itself, provided the data for P' only are used. This has been confirmed by Bergmann and Bergmann (*J. Amer. Chem. Soc.*, 1940, **62**, 1699) for 2-*iso*propenylanthracene. 1- and 2-Vinylanthracene have the smallest values of P for the positions 2 : 2′ and 2 : 1′, respectively, so in these cases the values of P are so unreliable as to predict the most reactive pair of positions incorrectly. This appears to be the first definite evidence that the inclusion of the overlap integral in molecular orbital calculations of quantities such as resonance energies can improve the agreement with experiment even qualitatively.

The vinylphenanthrenes all have para-localisation energies such that addition should occur, 9-vinylphenanthrene being easily the most reactive. The latter has been found to add maleic anhydride at the expected positions (Bergmann and Bergmann, *ibid.*, 1937, **59**, 1443).

TABLE III.

Arylbutadienes.

Butadiene.	Position.	N.	P $(-\beta)$.	P' $(-\gamma)$.	P' kcals.	k_r.
Unsubstituted	1 : 4	1	2·47	1·77	60	1
1-Phenyl	1 : 4	2	2·04	1·96	67	2×10^{-4}
2-Phenyl	1 : 4	1	2·43	1·75	60	3
1-α-Naphthyl	1 : 4	2	2·06	1·97	67	10^{-4}
	2 : 2′	2	3·78	2·46	84	—
1-β-Naphthyl	1 : 4	2	2·04	1·96	67	2×10^{-4}
2-α-Naphthyl	1 : 4	1	2·43	1·74	59	5
2-β-Naphthyl	1 : 4	1	2·44	1·75	60	3
1-9′-Anthryl	1 : 4	2	3·00	2·00	68	10^{-4}
2-9′-Anthryl	1 : 4	1	2·43	1·74	59	5
	9′ : 10′	3	3·75	2·23	76	—

TABLE IV.

Molecule.	N.	P $(-\beta)$.	P' $(-\gamma)$.	P' kcals.	k_r.
1-Phenyl-1-9′-phenanthrylethylene	1	2·58	1·89	64	3×10^{4}
1-Phenyl-2-9′-phenanthrylethylene	2	3·11	2·12	72	0·06
1 : 2-Diphenyl-1-9′-phenanthrylethylene	2	3·48	2·23	76	10^{-4}
1 : 2-Diphenylbutadiene	2	2·91	1·94	66	2×10^{2}
1 : 3-Diphenylbutadiene	2	2·89	1·92	65	5×10^{2}
1 : 4-Diphenylbutadiene	3	3·39	2·13	72	0·03
2 : 3-Diphenylbutadiene	1	2·37	1·70	58	4×10^{2}
1 : 2 : 3-Triphenylbutadiene	2	2·85	1·89	64	3×10^{4}
1 : 2 : 4-Triphenylbutadiene	3	3·37	2·11	72	0·1
1 : 2 : 3 : 4-Tetraphenylbutadiene	3	3·33	2·08	71	0·6
1-Phenyl-4-4′-diphenylylbutadiene	3	3·40	2·13	72	0·03

The para-localisation energies of some arylbutadienes are listed in Table III. From the results it is apparent that they are all very reactive, so instead of giving the " theoretical rates " relative to anthracene, the rates relative to butadiene, k_r, have been listed. It will be noticed that addition is most favoured if the aryl portion is attached to the butadiene by the most reactive position in the former and the less reactive position in the latter. This is due to the correlation between self-polarisabilities and chemical reactivities on the one hand, and the quantitative correlation of the former with conjugation energies (Brown, *Australian J. Sci. Res.*, 1949, *A*, **2**, 566) on the other. The experimental data do not permit a comparison of relative reactivities, but it has been found that 1-phenylbutadiene adds maleic anhydride very readily (Diels, Alder, and Pries, *Ber.*, 1929, **62**, 2081), that 6-methoxy-1-vinyl-3 : 4-dihydronaphthalene, which is approximately equivalent to 2-phenylbutadiene, is reactive even at room temperature (Dane, Höss, Bindseil, and Schmitt, *Annalen*, 1937, **532**, 39), and that 1-α-naphthyl-1 : 3-butadiene undergoes 1 : 4- rather than 2 : 2′-addition (Arnold and Coyner, *J. Amer. Chem. Soc.*, 1944, **66**, 1542).

When several aryl groups are attached to the one polyene, the possibility arises of steric interactions preventing the molecule assuming a configuration favourable for addition. Some such molecules are considered in Table IV. The first three compounds listed would be expected

to be reactive, although probably less so than anthracene, as judged solely by the respective para-localisation energies, the reactive positions being the ethylene carbon and the 10′-phenanthrene carbon atom in each case. Scale drawings of these reveal that the first and the third would exist preferably in the chair form (for the reactive four-carbon system) when planar, 1-phenyl-2-9′-phenanthrylethylene being the only one for which the planar boat configuration does not involve excessive hydrogen interactions. This is in agreement with the observation (Bergmann and Bergmann, *locc. cit.*) that, of the three, only the last compound added maleic anhydride. A similar interpretation seems reasonable for Craig's work on *cis*- and *trans*-piperylene (*J. Amer. Chem. Soc.*, 1943, **65**, 1006; cf. Norton, *Chem. Rev.*, 1942, **31**, footnote, p. 349), rendering questionable its support of a two-stage addition mechanism for the Diels–Alder reaction (Dewar, " Electronic Theory of Organic Chemistry," p. 151).

TABLE V.

The αω-diphenylpolyenes.[•]

Diphenylpolyene.	Position.	P $(-\beta)$.	P'. $(-\gamma)$.	P'. kcals.	k_a.
Butadiene	1 : 4	3·39	2·13	72	0·03
Hexatriene	1 : 4	3·48	2·20	75	5×10^{-4}
Octatetraene	1 : 4	3·47	2·20	75	5×10^{-4}
	3 : 6	3·56	2·27	77	1×10^{-4}
Decapentaene	1 : 4	3·44	2·18	74	0·002
	3 : 6	3·55	2·26	77	2×10^{-4}
Dodecahexaene	1 : 4	3·41	2·16	73	0·005
	3 : 6	3·53	2·25	76	3×10^{-4}
	5 : 8	3·54	2·26	77	2×10^{-4}

[•] For all additions considered in this table, N is 3.

TABLE VI.

The 1-phenylpolyenes.

Polyene.	N.	Position.	P $(-\beta)$.	P' $(-\gamma)$.	P' kcals.	k_a.
Ethylene	1	2 : 2′	3·44	2·42	82	10^{-9}
Butadiene	2	1 : 4	2·94	1·96	67	500
Hexatriene	3	1 : 4	3·47	2·18	74	0·02
	2	3 : 6	3·05	2·04	69	5
Octatetraene	3	1 : 4	3·54	2·24	76	5×10^{-4}
	3	3 : 6	3·59	2·27	77	10^{-4}
	2	5 : 8	3·07	2·06	70	2

Of the four diphenylbutadienes, the 1 : 3- and the 1 : 4-isomer can assume the requisite planar boat structure, so it is to be expected that these will add maleic anhydride, the former more readily than anthracene, the latter perhaps less readily [for this N is 3, so a direct comparison of P' with that of anthracene, for which N is 2, is not permissible (see Part I, also discussion above)]. Kuhn and Wagner-Jauregg (*Ber.*, 1930, **63**, 2662) found that 1 : 4-diphenylbutadiene gave a mixture of isomeric adducts; 1 : 3-diphenylbutadiene does not seem to have been studied. The 1 : 2- and 2 : 3-diphenylbutadienes are probably not coplanar either for boat or for chair configurations of the butadiene system. However, this presumably is not sufficient to inhibit the (otherwise very ready) addition, because Bergmann and Bergmann found that 1 : 2-diphenyl-4-methylbutadiene was reactive, and 2 : 3-diphenylbutadiene has been found to react even in benzene (Allen, Eliot, and Bell, *Canadian J. Res.*, 1939, **17***B*, 75).

The sequence 1 : 2 : 4-triphenyl-, 1 : 2 : 3-triphenyl-, 1 : 2 : 3 : 4-tetraphenyl-butadiene represents increasing steric opposition to the assumption of a planar boat configuration. The fact that the first does and the last does not add maleic anhydride (Bergmann and Bergmann, *J. Amer. Chem. Soc.*, 1940, **62**, 1699; Bergmann, Winter, and Schreiber, *Annalen*, 1933, **500**, 122) in spite of the opposite tendencies as evinced by the para-localisation energies demonstrates again the importance of these steric considerations. It seems likely, in view of its very low para-localisation energy, that 1 : 2 : 3-triphenylbutadiene will add maleic anhydride fairly readily, but the uncertainty about steric conditions precludes any more definite prediction.

The last compound in Table IV should from the theoretical results be very similar in reactivity to 1 : 4-diphenylbutadiene. It has been shown to react with maleic anhydride in excellent yield (Bergmann and Weizman, *J. Org. Chem.*, 1944, **9**, 415).

The diphenylpolyenes (Table V) present some interesting results. Of the lower members of the series, diphenylbutadiene is the most reactive and diphenylhexatriene the least; the reactivity then slowly increases, tending to that of diphenylbutadiene. Addition of one mole of maleic anhydride to diphenyloctatetraene yields an adduct containing a conjugated system equivalent to that of 1-phenylbutadiene. The latter adds another mole of maleic anhydride to give the di-adduct more rapidly than the original molecule, as judged from the respective values of P', so it should only be possible to detect the di-adduct, even with a deficit of anhydride, as observed by Kuhn and Wagner-Jauregg (*loc. cit.*). Diphenyldecapentaene again is most reactive at the 1 : 4-positions, the mono-adduct containing the 1-phenylhexatriene system. As seen from Table VI, this is most reactive at the 3 : 6-positions and again only the di-adduct would result. Kuhn and Wagner-Jauregg claimed to prove that the di-adduct is formed by 1 : 4- and 7 : 10-additions (corresponding to 1 : 4-addition in the phenylhexatriene portion) by converting it into di-4′-diphenylylethylene; however, they describe two different di-adducts and it is not clear whether the proof applies to both or not. Also in molecules such as diphenyldecapentaene reactivity of certain positions is dependent upon favourable steric conditions which may not be attainable.

Conclusion.—The theoretical results just considered again afford a satisfactory interpretation of the available experimental results. In some cases the theoretical predictions are less certain owing to lack of knowledge of the precise stereochemistry of the molecule in question. For some molecules, where the question is mainly that of approximate coplanarity or not, the latter could perhaps be decided by spectrographic studies; however, it would first be necessary to establish whether coplanarity of the 4-carbon system involved in the reaction is required for addition. When the chair structure is more stable, the activation energy for chair–boat conversion will be one of the factors determining whether addition will occur at a reasonable rate. In cases where the alternative boat structure involves steric interactions, there seems little hope of discussing the Diels–Alder properties by the present simple theory, but when these are absent it may prove possible to extend the present theory by use of quantities B_4 and B_4' (the energies required to convert a given bond of a conjugated system into a pure single bond) which are calculable in a manner very similar to that used for P and P'.

In the above discussion of theoretical data it emerged that P' was more reliable than P when considering the Diels–Alder properties of arylpolyenes. This may possibly be connected with the fact that the resonance energies of polyenes, computed with $S = 0$, seem to be too great. For example, the values of β and γ deduced from Dewar's data (*loc. cit.*) for benzene, naphthalene, and anthracene are $-17._1$ and $-33._6$ kcals., respectively. These parameters lead to the following resonance energies (kcals.):

	From R.	From R′.		From R.	From R′.
Butadiene	8	6	Hexatriene	17	13

whereas data from heats of hydrogenation (Wheland, "The Theory of Resonance," p. 56), although not completely reliable (cf. discussion by Dewar, *loc. cit.*), indicate values around 4 kcals. for butadiene. Thus there is probably a variable over-estimation of the stability of polyenes, and possibly also in smaller degree for arylpolyenes, when using R, and this will result in P being too small an estimate of the para-localisation energy when the r.m. contains polyene systems in place of cyclic systems in the original molecule. Hence P will indicate too great a reactivity for molecules such as styrene, for which the r.m. is hexatriene for the most reactive pair of positions.

Similar considerations do not apply to the polycyclic hydrocarbons considered in Part I because for these the r.m. are also cyclic systems. For the polyenes, both original and residual molecules contain polyene systems, so this effect may cancel out to some extent. The underlying cause of the discrepancies for polyenes and arylpolyenes is doubtless the unsystematic variation of σ-bond energies accompanying addition as opposed to the systematic variation for polycyclic hydrocarbons.

In subsequent papers phenyl derivatives of aromatic systems, together with extensive theoretical data for polycyclic systems for subsequent experimental testing, will be considered.

UNIVERSITY OF MELBOURNE, VICTORIA, AUSTRALIA. [*Received, April 24th*, 1950.]

526. *Studies of Gradual Transitions in Mixed Crystals. Part I. The System Ammonium Chloride–Ammonium Bromide.*

By C. J. Mandleberg and L. A. K. Staveley.

The volume-temperature relationships for mixed crystals of ammonium chloride and ammonium bromide have been determined between room temperature and *ca.* −110° with the object of investigating the effect of mixed-crystal formation on the gradual transitions (λ-points) in these two salts. The λ-point for pure ammonium chloride (242·5° K.) is depressed by the replacement of chloride by bromide ions, the temperature of the transition falling off increasingly rapidly and reaching 212·2° K. at 11·6 moles % of bromide. At about 8 moles % of bromide an upper transition appears, similar to that in pure ammonium bromide, in that it involves a contraction when the crystal is heated. For a range of a few units % of ammonium bromide, therefore, the mixed crystals display two successive transitions, but above 15 moles % of this salt, the lower can no longer be detected. Thereafter, the temperature of the bromide-like transition rises to a maximum at about 50 moles % of ammonium bromide, and then falls to the value for the pure salt. These results are considered in the light of existing knowledge of the nature of transitions in ammonium halides, the gradual transitions in which are regarded as representing changes from a state in which the cations undergo torsional oscillations, to one in which, while this motion continues to be predominantly of the same kind, they can occasionally change from one orientation to another. This type of motion we have called quasi-rotation. Reasons are given for believing that in the mixed crystals the N–H · · · Br interaction gives rise to a stronger orienting force on the ammonium ions than do the N–H · · · Cl interactions, and that the phenomenon displayed by the mixed crystals is due essentially to the decreased symmetry of the field of force acting on a cation, compared with that in the pure salts. In particular, it is suggested that in the region of composition where the system displays two transitions, the cations achieve quasi-rotational freedom in two stages, first about the N–H · · · Br axes at low temperatures, and finally in three degrees of freedom at the upper temperature.

Although many of the gradual transitions (λ-points) occurring in pure solids have been carefully investigated, relatively little work has so far been carried out on binary mixed crystals in which one or both of the components exhibit such a transition. Since mixed-crystal formation involves an alteration in the molecular or ionic environment in the lattice, which must necessarily have repercussions on what are essentially co-operative phenomena, it would seem that studies of such binary systems should provide one useful experimental line of attack on the problem of the nature and causes of these gradual transitions. Interesting results have in fact been obtained from the very few complete investigations of this kind which have already been carried out, such as those on the systems methane–krypton (Eucken and Veith, *Z. physikal. Chem.*, 1936, *B*, **34**, 275) and methane–tetradeuteriomethane (Bartholomé, Drikos, and Eucken, *ibid.*, 1938, *B*, **39**, 371).

In this paper are presented the results of what, it is hoped, will be the first of a series of investigations on solid solutions of two components of which one or both possess a λ-point. The system ammonium chloride–ammonium bromide was chosen as the first subject for study since there already exists a considerable amount of information about the transitions in these salts, and because they form a complete series of mixed crystals. The only previous observation relating to transitions in mixed crystals of these two salts seems to be that of Crenshaw and Ritter (*ibid.*, 1932, *B*, **16**, 143), who found by heat-capacity measurements that there is a gradual transition in a mixed crystal of approximately equimolecular proportions which lies at a higher temperature than the λ-points in the two pure compounds.

Experimental.

A dilatometric method is perhaps best suited to exploratory investigations of gradual transitions, since it lends itself both to the accurate determination of their temperatures, and to the investigation of any attendant hysteresis. Moreover, the particular system ammonium chloride–ammonium bromide has the additional interest that the volume changes occurring at the transition in the pure substances have opposite signs.

Smits and his co-workers have carried out very careful dilatometric studies on pure ammonium halides, in an apparatus designed for the intensive examination of any one salt (Smits and MacGillavry, *ibid.*, 1933, *A*, **166**, 97). Since an investigation of one given system of mixed crystals involves the successive study of several mixtures, we have used a simpler apparatus which permits of more rapid working over a range of temperature much wider than that investigated by Smits, at the expense of a slight loss in accuracy. It could in fact be emptied of one mixture, cleaned, and refilled with another in two days, and used for continuous observations between room temperature and −110°.

The dilatometer (Fig. 1) consisted of a bulb of about 50 c.c. capacity sealed to a calibrated capillary 120 cm. long, of internal cross-sectional area $1{\cdot}1 \times 10^{-6}$ sq. cm., terminating in a small tap. The bulb, in

which the salt under observation was contained together with the indicator liquid, had a thin-walled re-entrant glass tube, in which a thermocouple was placed. A side arm from the capillary led to a three-way tap through which the whole could be evacuated, or alternatively filled with liquid.

The thermostat consisted essentially of a cylindrical block of magnesium, 25 cm. long and 6 cm. in diameter, at the base of which was a small spike 1 cm. long. The dilatometer rested in a cavity in this block, and the block was suspended well inside a deep Dewar vessel containing liquid oxygen. This Dewar vessel was mounted on a platform the height of which could be varied with precision. To cool the block, matters were so arranged that the spike was either immersed in, or held just above, the liquid-oxygen surface. The block was wound with a heating coil, connected to the mains through a variable resistance. It could be held at a steady temperature by striking a balance between the current in the heating coil, and the height of the spike above the liquid oxygen surface.

The central cavity in the block, within which rested the bulb, had three vertical grooves disposed equiangularly in its side to receive copper tubes containing thermocouples. These grooves extended $\frac{1}{3}$, $\frac{2}{3}$, and the whole of the depth of the cavity, respectively. The block was suspended by a cord from three hooks, also equiangularly disposed, screwed into its upper face. One of the low-freezing non-inflammable mixtures recommended by Kanolt (*Sci. Papers Bur. Stand.*, 1924—1926, **20**, 619) was used to improve thermal contact between the bulb and the block.

When the dilatometer bulb was in position in the magnesium block, the capillary, which was etched with reference marks, lay flush against a steel metre scale which had previously been calibrated against a standard. The meniscus in the capillary was observed through an eyepiece.

To fill the dilatometer, it was inverted, and a weighed amount of solid introduced *via* a tube sealed to the base of the bulb. The tube was then drawn off 1 cm. from the bulb. The dilatometer was next turned right way up, and connected to a high-vacuum pump through the three-way tap which was lubricated with a dextrose–mannitol–glycerol grease. After being thoroughly evacuated, the dilatometer was filled with the degassed indicator fluid through the other limb of the tap. Toluene was first used as the indicator fluid, but in order to extend the experiments below −90°, it was discarded in favour of carbon disulphide (f. p. −111°). The liquids were purified by fractional distillation and dried over phosphoric oxide, and the dissolved air was boiled out.

The liquid level in the capillary could be adjusted by turning the three-way tap so that the liquid drained out, or by blowing more liquid into the capillary through the three-way tap by means of a hand bellows.

Temperature was measured with copper-constantan thermocouples, which were calibrated at the m.p.s of mercury, chloroform, *n*-heptane, and carbon disulphide, and also in liquid air (the temperature of which was measured with a carbon monoxide vapour-pressure thermometer). A calibration curve was constructed from these results and the data of Southard and Andrews (*J. Franklin Inst.*, 1929, **207**, 323). It was considered that these thermocouples then gave an absolute accuracy of temperature measurement of 0·1°, while temperature changes of a few degrees were estimated to 0·01°.

Three thermocouples were employed. One, in the re-entrant glass tube, was considered to give the temperature in the centre of the bulb. Another, in the groove extending $\frac{2}{3}$ of the way down the magnesium cylinder, gave the temperature of the block opposite the centre of the bulb. The third could be placed at various depths in the block, and used differentially to give information about the temperature gradient.

The apparatus was operated by placing the dilatometer in the block, reading on the scale the position of one of the reference marks on the capillary, and placing the Dewar vessel round the block. The mouth of the Dewar vessel was heavily lagged both inside and outside. (Such lagging was essential to the establishment of temperature uniformity through the magnesium block. Temperature differences between the ends of the block were, in fact, not more than 0·1°.) The indicator fluid was then pumped to the top of the capillary. The position of the liquid-air level relative to the block, and the heating current, were adjusted until the reading of the thermocouple in the block was steady. The readings of the thermocouple in the re-entrant tube, and of the meniscus in the capillary, were recorded when they became constant. The tap at the top of the capillary was momentarily opened before each reading to equalise the pressure within and without; otherwise it was kept shut to prevent loss from evaporation. The heating current was switched off, the block allowed to cool, and the process repeated at a suitable lower temperature. When, after several such readings, the liquid level approached the bottom

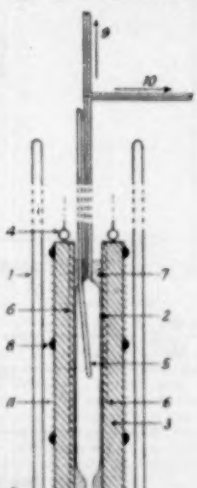


FIG. 1.

Dilatometer and thermostat: (1) ***Dewar vessel,*** (2) ***dilatometer,*** (3) ***magnesium block,*** (4) ***hook and cord suspension,*** (5) ***thin-walled glass tube for thermocouple,*** (6) ***grooves in block, at different depths, for thermocouples,*** (7) ***low-freezing liquid,*** (8) ***asbestos string for protection of Dewar vessel,*** (9) ***to calibrated capillary,*** (10) ***to three-way tap, connecting to pump and reservoir of dilatometer fluid,*** (11) ***heating coil.***

FIGS. 2—11.

Variation with absolute temperature of the molar volume of the pure salts and mixed crystals. *The quantity plotted as ordinate is* $V_T - V_0$, *where* V_T *is the volume in c.c. at* T° K. *of one mole of solid of composition specified, and* V_0 *is the volume of the same quantity at the ice-point. The open circles relate to runs in which the salt was being heated, the full circles to those in which it was being cooled.*

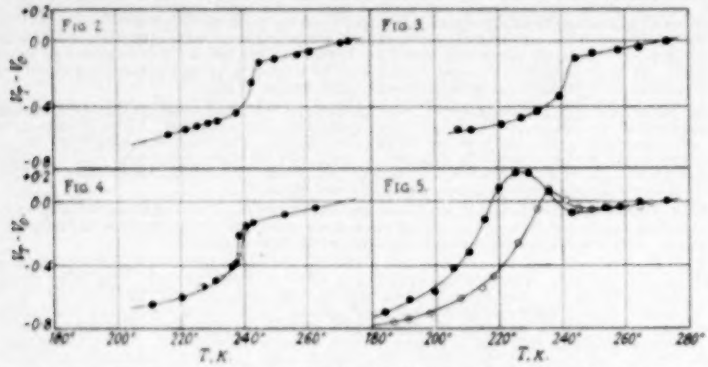


FIG. 2. *Pure* NH_4Cl. FIG. 3. 1·5 *Moles* % *of* NH_4Br. FIG. 4. 3·5 *Moles* % *of* NH_4Br.
FIG. 5. 8·5 *Moles* % *of* NH_4Br.

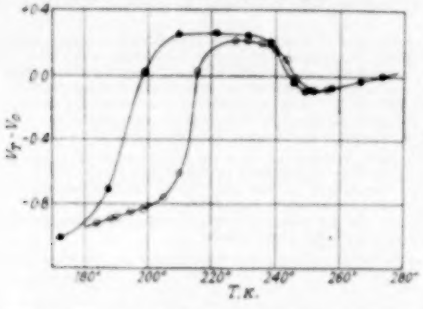


FIG. 6. 11·6 *Moles* % *of* NH_4Br.

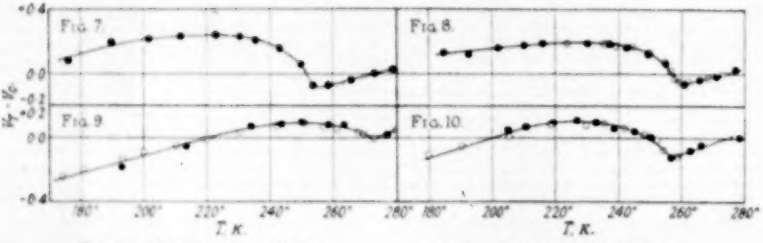


FIG. 7. 15·4 *Moles* % *of* NH_4Br. FIG. 8. 21·3 *Moles* % *of* NH_4Br.
FIG. 9. 59·8 *Moles* % *of* NH_4Br. FIG. 10. 84·8 *Moles* % *of* NH_4Br.

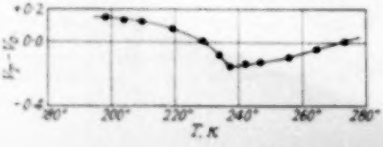


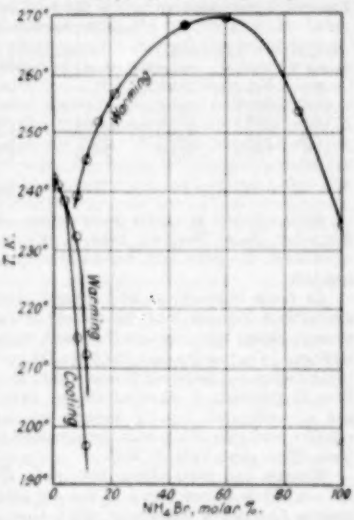
FIG. 11. *Pure* NH_4Br.

of the scale, the temperature was held constant while a reading was taken as described above, the liquid was pumped to the top of the capillary, and a second reading taken at the same temperature. When the lowest desired temperature had been attained, the procedure was reversed, and a heating run was carried out. When several such runs had been undertaken on each sample investigated, the dilatometer was removed from the block, the drawn-off tube cut off, the bulb emptied, and a new tube sealed on, before it was cleaned and refilled.

"AnalaR" ammonium chloride was used without further purification, and ammonium bromide was obtained by twice recrystallising the purest sample available. The mixed crystals were made by slow recrystallisation from solutions containing various proportions of the two salts. After being dried at 120° (cf. Crenshaw and Ritter, *loc. cit.*), they were heated in a sealed tube at 180° for 10—12 hours to ensure their homogeneity. The evidence for believing that this treatment does in fact give homogeneous mixed crystals is as follows: (1) Crenshaw and Ritter found that mixed crystals made by this method behaved in their calorimetric experiments identically with those which had been kept in the mother-liquor under isothermal conditions long enough to achieve equilibrium. (2) Havighurst and Mack (*J. Amer. Chem. Soc.*, 1925, **47**, 29) reported that their *X*-ray diffraction patterns of mixed crystals made by this method were those of homogeneous crystals. (3) The transitions in crystals containing more than 20% of ammonium bromide were no more diffuse than those in the pure salts; the behaviour of the chloride-rich mixtures is discussed below. (4) A sample mixed crystal was progressively dissolved after being subjected to the above thermal treatment: there was no change in the chloride/bromide ratio of the residue after each dissolution.

FIG. 12.

Variation with composition of the temperatures of transitions in mixed crystals of NH_4Cl *and* NH_4Br. *The full circle gives the transition temperature found by Crenshaw and Ritter* (loc. cit.) *in the one mixture which they studied calorimetrically.* (0° C. = 273·10° K.)



There was, moreover, no indication that there was any tendency towards a separation of the components when a mixed crystal was cooled to low temperatures. That the homogeneity persisted was shown by (1) the perfect reproducibility of the results on every sample right from the first run; (2) the examination of *X*-ray powder photographs of two samples of mixed crystals with 8·5% of ammonium bromide, one of which had never been cooled below room temperature whereas the other had been cooled to −90°. These two photographs (which were kindly taken for us by Mr. H. M. Powell) were indistinguishable.

The mixed crystals were analysed by titrating portions of solutions of known strength with standard silver nitrate. There is a linear relation between the molar percentage of any one halide and the ratio of the weight concentration of a solution of the mixed crystals to the titre of standard silver nitrate for a fixed volume of this solution.

In order to find the variation with temperature of the volume of the salt, it is necessary to know as accurately as possible the volume of the fluid in the bulb at one temperature. As the bulb had to be opened and resealed for the investigation of each sample, its internal volume varied somewhat from one set of experiments to another. For this reason, and also because of the difficulties inherent in any method of finding directly the volume of fluid introduced into the bulb, this was estimated as follows. The volume of the solid was derived from its known mass and its density, which for the mixed crystal was calculated on the basis of Havighurst and Mack's statement (*loc. cit.*) that the side of the cubic unit cell in this system varies linearly with composition. Careful measurements were made of the rate of change of volume of the salt plus fluid in the neighbourhood of room temperature, *i.e.*, above the region of the transitions. That part of the expansion due to the salt was assessed for pure ammonium chloride and bromide from Simon and Bergmann's coefficient of expansion data (*Z. physikal. Chem.*, 1930, *B*, **8**, 255), and for the mixed crystals on the assumption that the coefficient of expansion is a linear function of composition. From the rate of volume change due to the fluid alone, its volume was determined, using for toluene the density data of Timmermans (*Sci. Proc. Roy. Dublin Soc.*, 1912, **13**, 310) and for carbon disulphide the coefficient of expansion results of Seitz, Alterthum, and Lechner (*Ann. Physik*, 1916, **49**, 85). The expansion effects due to the fluid are relatively so large that in calculating, by what is essentially the reverse of the procedure just described, the change in volume of the salt below 0°, allowance must be made for the fact that the latter changes slightly the volume of fluid in the bulb.

The results are shown graphically in Figs. 2—11. These have been plotted from a representative selection of a large number of experimental points, and show the variation with absolute temperature T of the quantity $V_T - V_0$, where V_T is the volume in c.c. at $T°$ K. of one mole of solid of composition specified, and V_0 the volume of the same quantity at the ice point.

Although a study of hysteresis was not a primary object of the investigation, and although the measurements were not sufficiently precise for the examination of very small effects of this kind, it may be stated that in the mixed crystals containing more than about 20% of ammonium bromide, the hysteresis accompanying the transition was not markedly greater than that for the pure salts. On the other hand, in the two mixtures which were found to undergo two transitions (*i.e.*, those containing 8·5 and 11·6% of NH_4Br; Figs. 5 and 6, respectively) there was very pronounced hysteresis. There was nothing to suggest that in these regions of large hysteresis the establishment of equilibrium was unusually slow; on reaching a particular temperature the dilatometer reading soon settled down to a steady value which showed no alteration after a period of 3 or 4 hours. It is interesting that for mixed crystals containing 8·5 and 11·6% of ammonium bromide the volume which a given mass of the solid occupies at 0° can be reproduced at no less than four lower temperatures.

The transition temperatures have, as usual, been regarded as those at which dV/dT is a maximum or a minimum. In order to determine them as accurately as possible, runs were carried out with small temperature increments or decrements (usually about 0·1° or 0·2°), and the transition temperature taken as the mean value of the temperatures for the interval showing the maximum or minimum dV/dT values. The transition temperatures are summarised in the Table. The figures for the two pure salts are in close agreement with the accurate values of Smits and his co-workers (NH_4Cl, Smits and MacGillavry, *loc. cit.*; NH_4Br, Smits, Ketelaar, and Muller, *Z. physikal. Chem.*, 1936, *A*, **175**, 359). In Fig. 12 the transition temperatures are plotted against the molar percentage of bromide. It will be seen that the transition temperature for the one mixed crystal studied calorimetrically by Crenshaw and Ritter is completely consistent with our own results.

Transition temperatures (K.) *of the pure salts and of mixed crystals of ammonium chloride and ammonium bromide* (0° C. = 273·10° K.).

NH_4Br, moles %	Expansion: cooling.	Expansion: warming.	Contraction: cooling.	Contraction: warming.	NH_4Br, moles %	Expansion: cooling.	Expansion: warming.	Contraction: cooling.	Contraction: warming.
0·0	242·2(3)°	242·5(5)°	—	—	15·4	—	—	250·5°	251·8°
1·3	240·8	241·1	—	—	21·3	—	—	256·7	256·7
3·5	238·1	238·6	—	—	59·8	—	—	269·1	269·5
8·5	215	232·5	238·5°	239·1°	84·8	—	—	253·7	253·8
11·6	196·6	212·2	244·0	245·2	100·0	—	—	234·3(0)	234·4

Discussion.

Although the available information about these transitions has been recently reviewed (Staveley, *Quart. Reviews*, 1949, **3**, 65) we shall restate briefly the essential facts about the λ-points in the pure salts before attempting to explain the observations made on the mixed crystals.

At room temperature and normal pressure, the stable forms of ammonium chloride and ammonium bromide both have body-centred cubic lattices. (These forms are designated II, since at higher temperatures they both change into a modification I each with face-centred cubic lattices.) On passing into the form III stable below the λ-point, the chloride retains its simple cubic lattice but becomes piezoelectric, so that III is in some way a less symmetrical structure than II (Hettich, *Z. physikal. Chem.*, 1934, *A*, **168**, 353). Ammonium bromide-III, however, has a tetragonal lattice, though of such dimensions that only slight changes in the relative positions of the ions are involved in the transformation II ⟶ III (Weigle and Saini, *Helv. Phys. Acta*, 1936, **9**, 515).

Menzies and Mills (*Proc. Roy. Soc.*, 1935, *A*, **148**, 407) showed that the transformation II ⟶ III is accompanied in the chloride, but not in the bromide, by the appearance of a Raman line of low frequency, which they attributed to asymmetric lattice vibrations. Since the positive charge on an ammonium ion is no doubt largely localised on the hydrogen atoms, it is highly probable that the energetically preferred orientation of such an ion with respect to its halide neighbours is that in which each of the four hydrogen atoms is as near as possible to a neighbouring anion. In a simple cubic lattice there are eight halide ions cubically grouped round each nitrogen atom, and such a preferred orientation of the tetrahedral cation will then obtain when each diagonal of the cube is perpendicular to a face of the tetrahedron. Menzies and Mills suggested that in the low-temperature form of the chloride, the lattice was built up by the simple translation of the elementary cube, so that all ammonium ions (when in the mean position) are in all respects parallel to one another. The chloride ions, however, are now not symmetrically placed with respect to the ammonium ions, so that the existence of the low-frequency Raman line is explained. They further suggested that, in the bromide in the III-form, the ammonium cations in two adjacent elementary cubes are anti-parallel to each other, so that the nearest *edges* of these two tetrahedra are now *parallel* to one another and not *perpendicular* as in the chloride.

If, in the chloride, the ammonium ions acquire mutually disordered orientations, or com-

mence to rotate, or if the amplitude of the torsional oscillations increases sufficiently, the lattice gains in symmetry, and both the low-frequency Raman line and also the piezoelectric properties disappear. A further consequence of this change in motion of the cations, however, is that it will tend to reduce the average distance between the hydrogen atoms of adjacent ammonium ions, and since these ions carry similar charges and thus tend to repel one another, the inter-ammonium repulsion will be thereby enhanced, and the lattice accordingly constrained to expand. A similar change in the bromide, however, involves a decrease in the average distance which separates the hydrogen atoms of neighbouring cations and hence results in a contraction of the lattice in virtue of the decreased inter-ammonium repulsion. In this way Menzies and Mills accounted for the striking fact that, although the gradual transitions in ammonium chloride and bromide are in many respects very similar, they differ in that the volume changes which accompany them are in opposite directions. It is important to stress that it is not necessary to postulate that in these salts the ammonium ions freely rotate in form II, for more recent evidence indicates that, for the chloride at least, cations do *not* in fact gain rotational freedom in the neighbourhood of the λ-point. The c_v values for ammonium chloride are only consistent with a librational or rocking movement of the ions both above and below the λ-point (Lawson, *Physical Rev.*, 1940, **57**, 417), and this conclusion is supported by nuclear magnetic resonance experiments (Bitter *et al.*, *ibid.*, 1947, **61**, 738).

We shall therefore suppose that in the III-forms of both salts the ammonium ions are constrained to librate with small amplitudes about ordered axes, the orienting forces being provided by the N–H · · · Hal interactions, and the mean position in each salt being that in which any one hydrogen atom is collinear with a nitrogen and a halogen ion. Furthermore, it will be assumed that in the form of the pure salts stable above the λ-points the torsional oscillation of the cations now occurs about disordered axes, that the amplitude of the oscillation is somewhat increased, and that occasionally an ammonium ion changes from one to the other of its two possible equilibrium positions within an elementary cube. (It may be noted that at transitions in molecular crystals composed of polar molecules, the change to the high-temperature form is often accompanied by a considerable increase in dielectric constant, showing that the molecules gain considerably in orientational freedom though they need not necessarily rotate in the high-temperature form.) Since the properties of forms II are in many ways what would be expected if the cations had the spherical symmetry which free rotation would give them, we shall speak of the motions of these ions as quasi-rotational.

The gradual transitions must therefore be regarded as essentially co-operative phenomena arising from a gradual change from purely librational to quasi-rotational motion, the region of temperature in which they are observed to occur depending primarily on the strength of the orienting forces. Since the transitions in the chloride and the bromide reach completion at temperatures only a few degrees apart, it would seem that the orienting forces in the two lattices are very nearly of the same strength, in spite of the fact that the distance of closest approach of a nitrogen and a bromine atom in the bromide (3·505 A. at room temperature) is greater than that of a nitrogen and a chlorine atom in the chloride (3·34 A.). Now Havighurst and Mack's *X*-ray studies (*loc. cit.*) established that the length of the side of the unit cell in mixed crystals of the two salts varies linearly with the composition. In any mixed crystal, therefore, the minimum N · · · Br distances are less, and the N · · · Br interactions stronger than in the pure bromide, while the minimum N · · · Cl distances must be greater and therefore the N · · · Cl interactions weaker than in the pure chloride. Accordingly, any NH_4 ion in a mixed crystal of these two substances is in a less symmetrical field of force than a cation in either of the pure salts. In particular, there is a preference for the N–H bonds to be aligned in the direction of bromide rather than chloride ions, and we consider that this is fundamentally responsible for the phenomena we have observed in the mixed crystals.

If we start with the pure bromide, and replace some of the anions by chloride ions, the orienting forces on any one cation are strengthened in some directions and weakened in others. Up to 50 moles % of chloride it seems that the net effect is an increased restriction on the torsional freedom of the cations, since the transition temperature rises until this composition is reached. On further replacement, the decrease in the number of bromide ions is no longer outweighed by the increasing strength of the N–H · · · Br interactions and the transition temperature falls. So long, however, as each cation has at least two bromide ions among the eight nearest anion neighbours, its orientation in the unit cube will be determined by its interaction with the bromide ions. In mixed crystals containing more than about 25 moles % of bromide we should therefore expect that the preferred mutual orientations of neighbouring tetrahedra will be similar to that in the pure bromide, and hence that the transition II ⟶ III will be bromide-like

in the sense that it will involve a contraction, as is indeed the case. It is noteworthy that this transition in the mixed crystal is not appreciably any more diffuse than in the pure bromide. At very low bromide concentrations, however, the rate at which the transition is depressed by increasing the proportion of bromide is about the same as that at which the transition temperature for ammonium bromide is raised by introducing a little chloride. When the bromide content is very small, the majority of cations still have eight chloride ions as nearest neighbours, and presumably endeavour to retain the relationship which prevails in the pure chloride, so that the depression of the transition temperature is probably largely caused by the slight increase in the lattice dimensions which the introduction of the bromide ions produces. In the region of 5—12 moles % of bromide, however, the temperature of the (lower) transition falls much more rapidly as the substitution of bromide for chloride proceeds. This rapid change in behaviour, coinciding with the appearance of the upper transition (and, incidentally, with an enormous increase in the hysteresis associated with the lower transition), suggests that it is in this region that a fundamental alteration takes place in the type of inter-ammonium ion relationship which prevails in the lattice.

The situation in this range of composition is perhaps most readily apprehended if we consider a mixed crystal containing 12½ moles % of ammonium bromide, and which is ideal in the sense that the distribution of chloride and bromide ions throughout the whole lattice is as uniform as possible. Although such uniformity cannot prevail in a real mixed crystal, this idealised model serves to throw light on the most probable interionic relationships.

Any one ammonium ion has then seven chloride ions and one bromide ion as its nearest anion neighbours. It is convenient here to visualise as the unit, a group of eight elementary cubes with one central bromide ion in common. Owing to the strong N–H · · · Br interaction, it is reasonable to suppose that the preferred orientation of the eight tetrahedra of the group will be that in which each has an apex directed towards the bromide ion. This group of eight tetrahedra, with cubic symmetry, recalls the arrangement which Menzies and Mills (*loc. cit.*) postulated for the pure bromide, and suggests that even at these comparatively low bromide concentrations, the transition characteristics of the mixed crystals should begin to show some resemblance to those of ammonium bromide. There is, however, the difference that the bases of the tetrahedra opposite to those apices which are nearest to the bromide ions, are, as it were, less firmly anchored than the apices themselves. It is thus possible in principle for the tetrahedra to undergo limited quasi-rotational movement about the N–H · · · Br axis, while preserving the same relationship with regard to the bromide ion. This partial quasi-rotation will be opposed by the N–H · · · Cl interaction, but as these are weaker than in the pure chloride, the quasi-rotation should set in at a lower temperature than it does in the pure chloride. It is suggested, therefore, that the low-temperature transition in that range of mixed crystals where there are two gradual transitions is, in fact, a manifestation of the acquisition by the ammonium ions of quasi-rotational freedom about one axis only. The upper transition is considered to result from the extension of this quasi-rotational movement to all axes when the temperature has become sufficiently high for the strong N–H · · · Br interaction to be overcome.

We now consider the volume changes at these successive transitions. Since tetrahedra in adjacent elementary cubes with a common face have their nearest edges parallel, any increase in the amplitude of oscillation about the N–H · · · Br axis increases the separation of these pairs of hydrogen atoms, and thereby reduces their mutual repulsion, and encourages contraction. On the other hand, this increase in inter-hydrogen separation will not be as great as that produced by an enhancement of the oscillational freedom about an axis, say, at right angles to the N–H · · · Br direction. Furthermore, if we regard the idealised 12½ moles % of bromide solid as being formed by the simple translation of a cube which consists of eight elementary cubes with a bromide ion at the centre of the group, then along the cube diagonals the arrangement of the tetrahedra is :

–face–apex–apex–face–face–apex–apex–face–

In addition, the hydrogen atoms of any two consecutive faces in the series (whether separated by two apices or not) are "staggered." Quasi-rotation of the tetrahedra about these diagonals (*i.e.*, about the N–H · · · Br axes) will diminish the average separation of these hydrogen atoms, and encourage an expansion of the lattice. Pending a detailed quantitative treatment, we may therefore say that limited quasi-rotation of the kind described is not necessarily inconsistent with a net expansion of the solid. The contraction at the upper transition presumably depends, like that in the pure bromide, on the marked increase in the distance between hydrogen atoms of the tetrahedral edges adjacent and parallel to the face diagonals of the elementary cubes.

The change to full quasi-rotational motion (which produces the last effect) will also cause a separation of the eight hydrogen atoms at the apices of the eight tetrahedra which are directed towards a bromide ion, and the diminished repulsion between these hydrogen atoms will likewise contribute towards a shrinking of the lattice.

If the distribution of the two sorts of halogen ion throughout the lattice of a mixed crystal were always as uniform as possible the interpretation we have placed on the experimental evidence would require that all signs of a low-temperature chloride-like transition should vanish when the bromide concentration reaches 25 moles %. Although we were unable to follow it to the point of its disappearance, the experiments give the impression that at least it is not likely to persist to higher bromide concentrations. At the highest bromide concentration which it was positively detected in the dilatometric experiments, its temperature is falling rapidly with increasing percentage of bromide. In addition, cooling curves were obtained for the samples containing up to 21·3 moles % of bromide down to 135° K. While these showed the presence of low-temperature transitions in the mixtures containing up to 11·6 moles % of bromide, there was no sign of this in the curves for the crystals with 15·4% and 21·3% of bromide. Accordingly, if it still persists in these crystals, the transition occurs at a temperature below 135° K., or else it has become very diffuse, or the heat effects associated with it have become very small.

THE INORGANIC CHEMISTRY LABORATORY,
SOUTH PARKS ROAD, OXFORD.

[*Received, May 11th*, 1950.]

---

527. *Antibacterial Pteridines. 6 : 7-Dialkyl Derivatives of 2 : 4-Diaminopteridine.**

By N. R. CAMPBELL, J. H. DUNSMUIR, and M. E. H. FITZGERALD.

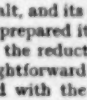
A series of 6 : 7-dialkyl-2 : 4-diaminopteridines * has been prepared; some of them exhibit high antibacterial activity against *Vibrio cholerae*.

DURING an investigation into the possibility of effective chemotherapeutic attack on cholera, we decided that derivatives of 2 : 4-diaminopteridine * were worthy of detailed study. Mallette, Taylor, and Cain (*J. Amer. Chem. Soc.*, 1947, **69**, 1814) have described the preparation of certain 6 : 7-disubstituted derivatives, including the dimethyl compound which has been found by Daniel *et al.* (*J. Biol. Chem.*, 1947, **169**, 689; 1947, **170**, 747) to show antibacterial activity against certain organisms, including *Bacterium coli* and *Staphylococcus aureus*. Although this 6 : 7-dimethyl-2 : 4-diaminopteridine was found not to possess any notable activity against *Vibrio cholerae*, we have now prepared and studied an extensive series of related pteridines with quite promising results.

Pteridines substituted by two identical alkyl groups are made most readily by interaction of tetra-aminopyrimidine, or one of its salts, with the appropriate aliphatic diketone. A suitable salt is the " bisulphite," prepared from 5-nitroso-2 : 4 : 6-triaminopyrimidine by reduction in aqueous suspension with sodium dithionite. This salt, and its method of preparation, have been dealt with by Mallette *et al.* (*loc. cit.*) and we have prepared it by their process, with certain modifications. We are, however, of the opinion that the reduction of nitrosotriaminopyrimidine in this manner is by no means a simple, straightforward reaction; the water-solubility and stability of the product are closely associated with the detailed experimental conditions employed.

Most of the members of this series of pteridines were prepared by reactions in the presence of acetic acid, but in certain cases it was found satisfactory to carry out the reaction in aqueous-alcoholic solution, in the presence of mild alkalis or organic bases.

With the exception of camphorquinone, the α-diketones used were all prepared by oxidation of the corresponding acyloins. The general method used for the preparation of these acyloins was that of Snell and McElvain (*Org. Synth.*, 1943, Coll. Vol. II, p. 114). The solvents employed were boiling ether or benzene at 40°; the former proved quite satisfactory for the shorter-chain members of the series, but when it was used with esters such as hexanoates and octanoates, reaction became retarded and was eventually stopped by the accumulation of insoluble material

* Numbering according to the Ring Index 

on the powdered sodium. Benzene did not share this disadvantage. Only ethyl phenylacetate failed to undergo this reaction; the required acyloin was later prepared by the interaction of benzylmagnesium chloride and acetaldehyde cyanohydrin.

Vibriostatic activities of 6 : 7-*dialkyl*-2 : 4-*diaminopteridines.*

Alkyl groups (at 6 and 7).	α-Diketone from which derived.	Minimal inhibitory dose (μg. per ml.).
H	Glyoxal	>500
Me	Diacetyl	>500
Et	Hexane-3 : 4-dione	40
Pr^n	Octane-4 : 5-dione	80
Pr^i	2 : 5-Dimethylhexane-3 : 4-dione	10
Bu^n	Decane-5 : 6-dione	>500
Bu^i	2 : 7-Dimethyloctane-4 : 5-dione	>500
sec.-Bu	3 : 6-Dimethyloctane-4 : 5-dione	40
n-Amyl	Dodecane-6 : 7-dione	>500
sec.-Amyl	4 : 7-Dimethyldecane-5 : 6-dione	>500
$CHEt_2$	3 : 6-Diethyloctane-4 : 5-dione	>500
n-Hexyl	Tetradecane-7 : 8-dione	>500
n-Heptyl	Octadecane-8 : 9-dione	>500
*cyclo*Hexyl	Dicyclohexyl diketone	>500
*cyclo*Hexylmethyl	1 : 4-Dicyclohexylbutane-2 : 3-dione	>500
Benzyl	1 : 4-Diphenylbutane-2 : 3-dione	>500
	Camphorquinone	80

As has been noted in the literature (particularly see Bouveault and Locquin, *Compt. rend.*, 1905, **140**, 1699), oxidation of acyloins to the α-diketones frequently affords poor yields. A variety of oxidising agents was tried in this work; chromium trioxide proved useful but the most encouraging results were obtained by the use of cupric acetate in diluted acetic acid (cf. Bloch, Lehr, Erlenmeyer, and Vogler, *Helv. Chim. Acta*, 1945, **28**, 1410).

Vibriostatic activities were determined by Dr. H. O. J. Collier, who will report the full biological work elsewhere. The table indicates the comparative activities of members of this series, when tested in a peptone–water medium against an inoculum of 10^9 vibrios (Madras 48210) per ml. at pH 7·2.

These results show a notable degree of specificity. Appreciable vibriostatic activity in the series appears to be restricted to those members which have aliphatic chains two or three carbon atoms in length; the activity is increased by addition of a methyl group on the α-carbon atom and decreased by a methyl group on the β-carbon atom. The effect of the α-methyl group is reversed on replacing it by an ethyl group.

The inactivity of the di*cyclo*hexyl derivative is fully in accordance with these observations and, although the exact relationship of the camphorquinone residue to these pairs of alkyl groups is somewhat complex, we consider the appreciable activity of the pteridine derived from camphorquinone to be quite compatible with the above generalisation.

Experimental.

Preparation of Acyloins and α-Diketones.—Acyloins were prepared from the appropriate esters by the method of Snell and McElvain (*loc. cit.*). Methods used for the oxidation of acyloins to α-diketones were as follows:

(I) Copper sulphate–pyridine, as described by Hartmann and Dickey (*J. Amer. Chem. Soc.*, 1933, **55**, 1228), but with 3 mols. of copper sulphate per mol. of acyloin.

(II) Copper acetate–acetic acid, as described by Bloch *et al.* (*loc. cit.*).

(III) Chromium trioxide, in an equal weight of water, added slowly to a cooled solution of the acyloin in acetic acid.

The following were prepared in the solvent or by the method named in parentheses: 4-*hydroxy*-3 : 6-*dimethyloctan*-5-*one* (ether) (72%), b. p. 95—100°/12 mm., n_D^{20} 1·439 (Found: C, 69·75; H, 11·8. $C_{12}H_{24}O_2$ requires C, 69·7; H, 11·7%), and 3 : 6-*dimethyloctane*-4 : 5-*dione* (II, 62%; III, 46%), b. p. 67—70°/12 mm., n_D^{20} 1·418 (Found: C, 69·7; H, 10·35. $C_{12}H_{22}O_2$ requires C, 70·55; H, 10·65%); 4-*hydroxy*-4 : 7-*dimethyldecan*-6-*one* (benzene) (75%), b. p. 110—115°/12 mm., n_D^{20} 1·441 (Found: C, 72·35; H, 11·95. $C_{13}H_{26}O_2$ requires C, 71·95; H, 12·10%), and 4 : 7-*dimethyldecane*-5 : 6-*dione* (III) (40%), b. p. 95—100°/12 mm., n_D^{20} 1·424 (Found: C, 72·85; H, 11·1. $C_{12}H_{22}O_2$ requires C, 72·7; H, 11·2%); 4-*hydroxy*-3 : 6-*diethyloctan*-5-*one* (benzene) (88%), b. p. 112°/12 mm., n_D^{20} 1·443 (Found: C, 71·7; H, 11·8. $C_{12}H_{24}O_2$ requires C, 71·95; H, 12·1%), and 3 : 6-*diethyloctane*-4 : 5-*dione* (II, 70%; III, 60%), b. p. 94—97°/12 mm., n_D^{20} 1·428 (Found: C, 72·75; H, 11·25. $C_{12}H_{22}O_2$ requires C, 72·7; H, 11·2%); 4-*hydroxy*-1 : 4-*dicyclohexylbutan*-3-*one* (ether) (68%), b. p. 117°/0·05 mm., n_D^{20} 1·490 (Found: C, 75·7; H, 11·0. $C_{16}H_{28}O_2$ requires C, 76·15; H, 11·2%), and 1 : 4-*dicyclohexylbutan*-2 : 3-*dione* (III, 60%), b. p. 100°/0·05 mm., m. p. 52° (Found: C, 77·1; H, 10·45. $C_{16}H_{26}O_2$ requires C, 76·75, H, 10·45%).

Preparation of Pteridines.—General method A. A mixture of tetra-aminopyrimidine " bisulphite " (0·01 mol.), the α-diketone (0·01 mol.), acetic acid (60%; 50 ml.), and alcohol (5 ml.) were heated together under reflux for 3 hours. The mixture was poured into water (200 ml.) and neutralised to bromothymol-blue (green). The crude precipitate was recrystallised from alcohol (lower members) or aqueous alcohol (higher members), charcoal being used as required.

General method B. A mixture of tetra-aminopyrimidine " bisulphite " (0·015 mol.), the α-diketone (0·01 mol.), water (30 ml.), alcohol (20 ml.), and the selected base (0·015 mol.) were heated together under reflux for about 1 hour or until diketone could no longer be observed refluxing with the solvent. The mixture was cooled and diluted with an equal volume of water. The crude precipitate was purified as before.

The following pteridines were prepared by the method stated in parentheses : 2 : 4-diaminopteridine (cf. Mallette, Taylor, and Cain, *loc. cit.*) (45%), m. p. 320° (decomp.); 2 : 4-diamino-6 : 7-dimethylpteridine (cf. *idem, ibid.*; also A, 80%) (recrystallised from 0·1*N*-hydrochloric acid, the resulting hydrochloride being heated with aqueous sodium hydrogen carbonate), m. p. 360°; 2 : 4-*diamino*-6 : 7-*diethylpteridine* (A) (43%) (recrystallised from alcohol), m. p. 268° (Found : C, 54·7; H, 6·4; N, 39·0. $C_{10}H_{14}N_4$ requires C, 55·0; H, 6·5; N, 38·5%); 2 : 4-*diamino*-6 : 7-*di*-n-*propylpteridine* (A) (42%) (recrystallised from alcohol), m. p. 202° (Found : C, 58·6; H, 7·35; N, 33·6. $C_{12}H_{18}N_4$ requires C, 58·5; H, 7·4; N, 34·1%); 2 : 4-*diamino*-6 : 7-*diisopropylpteridine* [A, 50%; B, 90% (sodium hydrogen carbonate)] (recrystallised from alcohol), m. p. 246° (Found : C, 58·4; H, 7·3; N, 34·2%); 2 : 4-*diamino*-6 : 7-*di*-n-*butylpteridine* [A, 40%; B (dimethylamine), 20%] (recrystallised from aqueous alcohol), m. p. 180° (Found : C, 61·0; H, 7·9; N, 30·0. $C_{14}H_{22}N_4$ requires C, 61·3; H, 8·1; N, 30·6%); 2 : 4-*diamino*-6 : 7-*diisobutylpteridine* (A) (30%) (recrystallised from aqueous alcohol, following chromatographic purification from chloroform–alcohol on alumina), m. p. 218° (Found : C, 61·05; H, 7·95; N, 30·8%); 2 : 4-*diamino*-6 : 7-*di*-sec.-*butylpteridine* (A) (21%) (recrystallised from aqueous alcohol, after precipitation by shaking a benzene solution of the crude gummy product with aqueous sodium hydrogen carbonate), m. p. 210° (Found : C, 61·2; H, 7·8; N, 30·8%); 2 : 4-*diamino*-6 : 7-*di*-n-*amylpteridine* (A, 15%; B, 15%) (recrystallised from aqueous alcohol), m. p. 160° (Found : C, 63·3; H, 8·6; N, 27·7. $C_{14}H_{22}N_4$ requires C, 63·5; H, 8·7; N, 27·8%); 2 : 4-*diamino*-6 : 7-*di*-sec.-*amylpteridine* [A, 8%; B (sodium hydrogen carbonate), 14%] (recrystallised from 0·1*N*-hydrochloric acid, the base being regenerated by treatment with hot aqueous sodium hydrogen carbonate and repeatedly recrystallised from alcohol), m. p. 172° (Found : C, 63·2; H, 8·5; N, 28·4%); 2 : 4-*diamino*-6 : 7-*di*-(1-*ethyl*-n-*propyl*)*pteridine* (A, 15%; B, unsuccessful) (recrystallised from aqueous alcohol), m. p. 181° (Found : C, 63·2; H, 8·7; N, 28·2. $C_{14}H_{22}N_4$ requires C, 63·5; H, 8·7; N, 27·8%); 2 : 4-*diamino*-6 : 7-*di*-n-*hexylpteridine* (A, 25%) (recrystallised from alcohol, after recovery from benzene solution, recrystallisation from 0·1*N*-hydrochloric acid, and treatment with aqueous sodium hydrogen carbonate), m. p. 140° (Found : C, 64·85; H, 9·2; N, 25·5%. $C_{14}H_{24}N_4$ requires C, 65·45; H, 9·15; N, 25·4%); 2 : 4-*diamino*-6 : 7-*di*-n-*heptylpteridine* (A) (28%) (recrystallised from aqueous alcohol), m. p. 132° (Found : C, 66·6; H, 9·4; N, 23·5. $C_{16}H_{28}N_4$ requires C, 67·0; H, 9·6; N, 23·45%); 2 : 4-*diamino*-6 : 7-*dicyclohexylpteridine* (A) (25%) (recrystallised from alcohol), m. p. 270° (Found : C, 65·8; H, 8·0; N, 26·0. $C_{18}H_{24}N_4$ requires C, 66·25; H, 8·05; N, 25·7%); 2 : 4-*diamino*-6 : 7-*di*(cyclo*hexylmethyl*)*pteridine* [A, 21%; B (dimethylaniline), 22%] (recrystallised from alcohol), m. p. 230° (Found : C, 67·65; H, 8·6; N, 23·7. $C_{20}H_{32}N_4$ requires C, 67·75; H, 8·55; N, 23·7%); 2 : 4-*diamino*-6 : 7-*dibenzylpteridine* (A) (20%) (recrystallised from alcohol), m. p. 258° (decomp.) (Found : C, 70·35; H, 5·05; N, 24·5. $C_{20}H_{18}N_4$ requires C, 70·2; H, 5·3; N, 24·5%).

2 : 4-*Diaminocamphano*(2′ : 3′- or 3′ : 2′-6 : 7)*pteridine.*—A mixture of camphorquinone (6 g.), tetra-aminopyrimidine " bisulphite " (8 g.), hydrochloric acid (4 ml.), alcohol (50 ml.), and water (140 ml.) was boiled under reflux for 4 hours. The mixture was cooled, the pH adjusted to 6, and the separated solid collected, extracted with boiling water, and dried. The *product* (7 g.), recrystallised from alcohol (with charcoal), had m. p. 305° (Found : C, 62·2; H, 6·65; N, 31·2. $C_{14}H_{18}N_4$ requires C, 62·4; H, 6·65; N, 31·1%).

We thank Dr. H. O. J. Collier for supplying the pharmacological results (Collier and Waterhouse, in the press) and the Directors of Messrs. Allen and Hanburys Ltd. for permission to publish this work.

Organic Chemical Department,
Allen and Hanburys Ltd., Ware, Herts.

[*Received, May 17th,* 1950.]

528. *Deoxypentose Nucleic Acids. Part I. The Enzymic Degradation of Sodium Deoxyribonucleate by Deoxyribonuclease.*

By W. G. Overend and M. Webb.

Deoxyribonuclease has been isolated from ox-pancreas according to McCarty's procedure (*J. Gen. Physiol.*, 1946, **29**, 123), and a number of its properties re-determined. As a first step the enzyme depolymerises deoxyribonucleic acid to smaller units which are then hydrolysed to acid-soluble polynucleotides. In contrast to the results of Fischer *et al.* (*J. pr. Chem.*, 1941, **158**, 79) it has been shown that the diffusible degradation products exhibit a wide range of molecular size. The enzyme hydrolyses preferentially the pyrimidine nucleotide groups of deoxyribonucleic acid and leaves a core which contains an increased ratio of purines to pyrimidines and resists further action of the enzyme.

Although the importance of deoxyribonucleic acids in the structure of living cells has been recognised for many years, the study of the properties of these macromolecules has been hampered to some extent by the lack of suitable methods for their isolation in the native (undegraded) form. The stimulation of interest in the properties, composition, and function of this class of compound which followed the introduction of such methods by Mirsky and Pollister (*Proc. Nat. Acad. Sci.*, 1942, **28**, 344) has led to renewed investigations (cf. Gulland *et al.*, *J.*, 1947, 1129, 1131, 1141; Chargaff *et al.*, *J. Biol. Chem.*, 1948, **176**, 715; 1949, **177**, 405; 1949, **178**, 531), which have conclusively shown that the structural formulæ originally proposed (Levene and Tipson, *Science*, 1935, **81**, 98; *J. Biol. Chem.*, 1935, **109**, 623) for deoxyribonucleic acid were over-simplified. Unfortunately, little information concerning the structure of deoxyribonucleic acids is as yet forthcoming from degradative experiments with chemical reagents, especially acidic reagents, owing to the extreme lability of nucleic acids of this type. In consequence attention has been directed to a study of the enzymic degradation of deoxyribonucleic acids. Moreover a survey of the literature reveals that, although many results of enzymic hydrolysis of deoxyribonucleic acid have been reported, little agreement exists between the results and theories put forward by the various authors (see Allen, *Ann. Rev. Biochem.*, 1941, **10**, 221; Loring, *ibid.*, 1944, **13**, 295; Gulland, *ibid.*, 1945, **14**, 175). Therefore, as part of a wider investigation of methods of degrading deoxyribonucleic acids, it was considered advisable initially to re-investigate the properties and mode of action of deoxyribonuclease. The results of this investigation are recorded in this communication (cf. Overend and Webb, *Research*, 1949, **2**, 99).

Preparation and Properties of the Enzyme.—The deoxyribonuclease was isolated from ox-pancreas in highly active form by essentially the method of McCarty (*J. Gen. Physiol.*, 1946, **29**, 123). [Since this work was completed, Kunitz (*Science*, 1948, **108**, 19) following McCarty's procedure has announced the crystallisation of deoxyribonuclease, but an investigation of the mode of action of this preparation was not reported.]

McCarty (*loc. cit.*) and other workers (Fischer *et al.*, *J. pr. Chem.*, 1941, **158**, 79; Greenstein *et al.*, *Cold Spring Harbor Symp. Quant. Biol.*, 1947, **12**, 64) have shown that magnesium ions are essential for the activity of deoxyribonuclease. McCarty found 0·003M-magnesium ion to be the optimal concentration for the activation of systems containing varying amounts of enzyme in the presence of a constant amount of nucleic acid. In similar conditions with our enzyme preparation the critical concentration of magnesium ion was *ca.* 0·001M. and little hydrolysis of the substrate occurred if the concentration was less than 0·0005M. In agreement with McCarty who found deoxyribonuclease to have optimum activity between pH 6·8 and 8·2, the present preparation had optimum activity between pH 7 and 8. Moreover our preparation, although considerably less stable than the corresponding ribonuclease (Kunitz, *J. Gen. Physiol.*, 1940, **24**, 15), appeared more stable than McCarty's preparation. The latter lost 90% of its activity after 15 minutes at 55° and at various pH values, and after one hour at this temperature no residual activity could be demonstrated. Our enzyme did not undergo rapid inactivation until heated above 80°. Under the given conditions and concentration of substrate (see Experimental section) little degradation of the nucleic acid occurred when the enzyme concentration was less than 10^{-4}%, whereas maximum degradation occurred when it was greater than 10^{-4}%. A detailed investigation of the action of inhibitors on deoxyribonuclease will be reported elsewhere. From the results obtained it seems that substances which inhibit the enzyme activity may be divided into two groups, namely, those which exert their action by removing the activating magnesium ions either by precipitation or by co-ordination, and those which directly react with the functional groups of the enzyme protein. Among substances of the first group we have

confirmed the inhibitory action of fluorides, citrates, and borates. Among those of the second group, thioglycollic acid markedly decreased the activity of deoxyribonuclease. Sulphydryl inhibitors such as iodoacetic acid and iodoacetamide had no effect on the enzyme.

The action of deoxyribonuclease on deoxyribonucleic acid results in an increase in titratable acid groups without the liberation of inorganic phosphorus. Fischer *et al.* (*loc. cit.*) claim that this increase in acidity corresponds to one acid equivalent (titrated to pH 9) for each four atoms of phosphorus initially present and presumes the formation of tetranucleotides. When his experiments were repeated with our enzyme preparation, the acid groups liberated by the enzyme action corresponded to only 0·503 acid equivalent per four atoms of phosphorus. Since intermediate values of 0·78 and 0·81 acid equivalent per four atoms of phosphorus have been obtained by Carter and Greenstein (*J. Nat. Cancer Inst.*, **1946**, **7**, 29) and by Zittle (*J. Franklin Inst.*, **1947**, **243**, 334; *Arch. Biochem.*, **1947**, **13**, 191) respectively, it is apparent that such measurements contribute little to interpretations of the mode of action of deoxyribonuclease.

FIG. 1. FIG. 2.

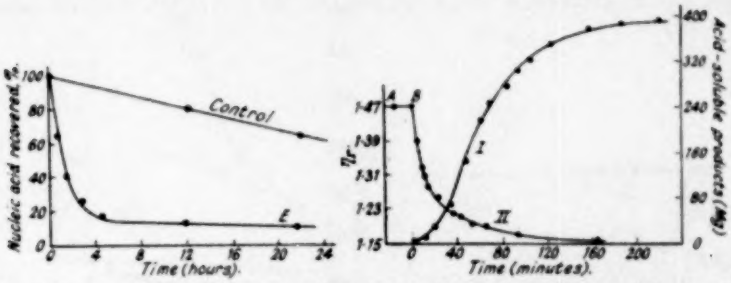


FIG. 1.—*Variation of deoxyribonuclease activity with time. Extent of the hydrolysis of thymus sodium deoxyribonucleate alone (control) and in the presence of deoxyribonuclease (curve E) at 37°.*

FIG. 2.—*Action of deoxyribonuclease on thymus deoxyribonucleic acid.*
Curve I. Formation of acid-soluble material. Curve II. Change in relative viscosity.
A—B shows that there is no change in viscosity before addition of enzyme.

Mode of Action of the Enzyme.—The variation of enzyme activity with time is shown in Fig. 1, which indicates that with 0·001% of enzyme and 1% of substrate the formation of acid-soluble material was complete within 5 hours. Fig. 2 shows the results obtained when more frequent determinations were carried out. [Control experiments indicated that, although prolonged incubation of the nucleic acid at pH 8 resulted in some non-enzymic hydrolysis (see Fig. 1), little (*ca.* 5%) formation of acid-soluble material, due to this cause, occurred during the first five hours.] It is seen that the formation of acid-soluble material does not occur to any marked extent in the first thirty minutes. It was observed, however, that during this lag period there was a rapid fall in viscosity of the substrate. This was essentially complete before the liberation of acid-soluble material became marked and obviously indicated a disaggregation of the deoxyribonucleic acid molecule. The changes in relative viscosity observed with the nucleic acids isolated from calf-thymus gland and herring sperm were considerably greater than the changes observed in solution of commercial (partly degraded) thymus deoxyribonucleic acid, but the solutions had approximately the same final relative viscosity. A full account of these results will be published later. From measurements of the influence of certain ions on the relative viscosities of solutions of the nucleic acid preparations used, it was concluded that the initial change in viscosity of enzyme–substrate systems (see Fig. 2) is caused entirely by the action of the enzyme and not by the non-specific action of ions, as has been suggested by Greenstein *et al.* (*loc. cit.*). Furthermore, no change occurred in the viscosity of a solution of the sodium deoxyribonucleate when 0·1M-magnesium sulphate was added, but a rapid decrease in the relative viscosity of the system followed the addition of a solution of the enzyme (0·002%) free from metallic ions. Moreover the disaggregation of the nucleic acid, as measured by the decrease in relative viscosity of the enzyme–substrate solution, was inhibited by the addition of sodium arsenate (see Fig. 3), which also inhibited the liberation of acid-soluble material (cf. Fischer *et al.*, *loc. cit.*). Since the viscosity measurements were carried out in the presence of 0·02M-magnesium

sulphate it appears probable that at this salt concentration the viscosity changes observed were not caused by disaggregation of the type recently suggested by Jungner *et al.* (*Nature*, 1949, **163**, 849). Thus it is concluded that the action of deoxyribonuclease on deoxyribonucleic acid results initially in the depolymerisation of the molecule to smaller units, which are subsequently hydrolysed to acid-soluble polynucleotides (cf. Greenstein and Jenrette, *Cold Spring Harbor Symp. Quant. Biol.*, 1941, **9**, 236).

Examination of "Acid-soluble" Polynucleotides.—Klein (*Z. physiol. Chem.*, 1933, **218**, 164) considered that the products of the enzymic (thymonuclease) degradation of deoxyribonucleic acid were simple mononucleotides, whereas Fischer *et al.* (*loc. cit.*) concluded that they were tetranucleotides, a conclusion accepted by Zittle (*loc. cit.*). Recent studies (cf. Gulland *et al.*, *loc. cit.*; Chargaff *et al.*, *loc. cit.*), however, conclusively show that the hypothesis of the "structural tetranucleotide" assumed by earlier workers is no longer completely acceptable. Consequently a large-scale enzymic hydrolysis of deoxyribonucleic acid was carried out and the products were examined.

FIG. 3. FIG. 4.

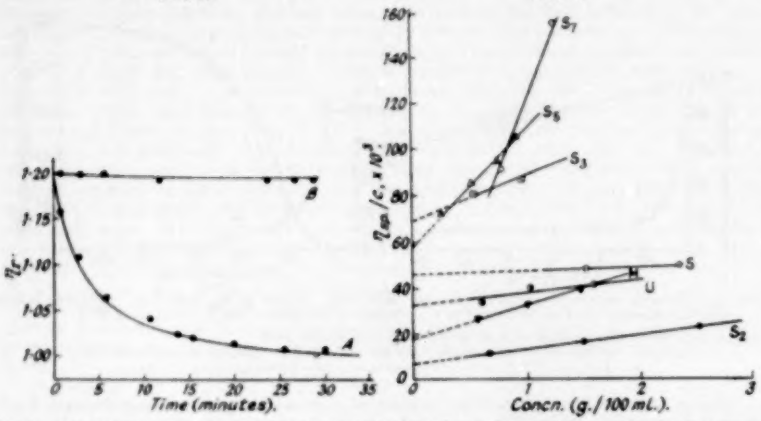


FIG. 3.—*Inhibition by sodium arsenate of the depolymerisation of thymus sodium deoxyribonucleate as measured by the decrease in relative viscosity (η_{sp}) of the enzyme–substrate solution. Substrate:* 1% (*w/v*) *sodium deoxyribonucleate* (2 *ml.*), 0·2M-*veronal buffer* (1 *ml.*), *and* 0·1M-*magnesium sulphate* (1 *ml.*) *with the addition of* 0·001% (*w/v*) *solution of deoxyribonuclease* (1 *ml.*) (*curve A*), *or a mixture of* 0·002% (*w/v*) *solution of deoxyribonuclease* (0·5 *ml.*) *and* 0·1N-*sodium arsenate* (0·5 *ml.*) (*curve B*).

FIG. 4.—*Variation of* η_{sp}/c *with concentration* (*c*) *shown by the products resulting from the action of deoxyribonuclease on deoxyribonucleic acid.*

(a) *Dialysis.* A preliminary dialysis served to separate the material into dialysable and non-dialysable components (fractions S and R respectively). Graded dialysis of S yielded a number of fractions (S_1—S_4) and a non-dialysable residue (S_7). The fact that a non-dialysable fraction (S_7) was obtained from a mixture which initially was separated by dialysis is attributed to the fact that the fractional dialysis was against repeated changes of distilled water which effectively removed metallic ions from the system. It is known that polynucleotides dialyse to a greater extent in the presence of ions (Lehmann-Echternacht, *Z. physiol. Chem.*, 1941, **269**, 169, 187, 201). Fischer *et al.* (*loc. cit.*) state that the products of the enzymic hydrolysis of deoxyribonucleic acid are completely precipitated from solution by acidic solutions of molybdate ions whereas mononbonucleotides, deoxyriboguanylic acid, and muscle adenylic acid are not precipitated. In contrast to these observations certain of the fractions (*e.g.*, S_1—S_4) which dialysed most readily and presumably were of relatively low molecular weight were not precipitated completely by acid-molybdate reagent. The soluble material could be precipitated by the subsequent addition of uranyl acetate in trichloroacetic acid, and by this means S_1 was separated into two portions (M and U respectively). Consequently the fractions separated by dialysis were far from homogeneous.

(b) *Controlled precipitation with ethanol.* The fraction S was further separated into five

fractions (O_1—O_4) by controlled precipitation with ethanol. It is thought that fractionation by this procedure results in the loss of much of the polynucleotide material of relatively high molecular weight, by co-precipitation with inorganic fractions. In consequence fractions O_5—O_8, which were free from inorganic salts, probably represent the lower polynucleotide degradation products.

(c) *Viscosities of the fractions.* The specific viscosities of aqueous solutions of the fractions were determined in Ostwald viscometers at 37·5°. Results (Fig. 4) confirm that the products of the enzymic hydrolysis are not homogeneous and differ widely among themselves with respect to molecular size. The absence of suitable polynucleotide reference compounds, together with the complex nature of the relationship between molecular size and viscosity of polyvalent acids of high molecular weight (Kern, *Z. physikal. Chem., Abs. A.*, 1938, **181**, 283; Owens, Lotzkar, Schultz, and Maclay, *J. Amer. Chem. Soc.*, 1946, **68**, 1628), do not justify any attempt to obtain a measure of the relative molecular weights of the various fragments from these results. However certain general conclusions may be drawn. The relative positions and slopes of the curves ($\eta_{sp.}/c$ plotted against c) for the fractions S_3, S_5, S_6, and S_7 confirm that they are of increasing molecular weight. It is also of interest that $\eta_{sp.}/c$ of these fractions decrease with

Fig. 5.

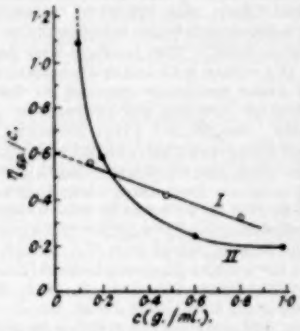


Fig. 6.

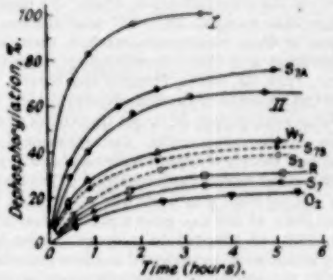


Fig. 5.—*Variation of $\eta_{sp.}/c$ with concentration (c) of deoxyribonucleic acids in water (I) and in 6% sodium chloride solution (II).*

Fig. 6.—*Liberation of inorganic phosphate by the action of prostate phosphatase on adenylic acid (I), adenosine–cytosine dinucleotide (II), and the products* (O_1, S_7, R, S_3, S_{7B}, W_1, S_{3A}) *resulting from the action of deoxyribonuclease on deoxyribonucleic acid.*

dilution as is the case with neutral polymers, whereas with the intact nucleic acid molecule $\eta_{sp.}/c$ increases with dilution (Fig. 5). This anomolous behaviour is shown by other strong polyelectrolytes (Fouss, *J. Polymer Sci.*, 1948, **3**, 603). With deoxyribonucleic acid the abnormal behaviour cannot be attributed solely to the electroviscous effect, since the relationship between $\eta_{sp.}/c$ and c is even more complex in the presence of an excess of salt, than in water alone (see Fig. 5).

(d) *Diffusion.* Results obtained with the apparatus described by Gage (*Trans. Faraday Soc.*, 1948, **44**, 253) indicate, in a general manner, the increasing molecular size of the dialysis fractions S_3, S_5, and S_4, and confirm the previous suggestion that the O-fractions contain the lower polynucleotides. [Anomalous values obtained with fractions S_{7B} (see later) and O_4 can only be attributed to the many sources of error associated with the measurements.] These results differ from those reported by Fischer *et al.* (*loc. cit.*) who measured absolute molecular weights. However it is considered that with polyelectrolytes of this type the diffusion method is unsuitable for accurate determination of molecular weight.

(e) *Action of prostate phosphatase* (cf. Schmidt, Cubilees, and Thannhauser, *Cold Spring Harbor Symp. Quant. Biol.*, 1947, **12**, 161, for analogous work on the products from the action of ribonuclease on ribonucleic acid). The work of Schmidt *et al.* (*loc. cit.*) shows that the amount of the total phosphorus liberated from a polynucleotide as inorganic phosphate by acid phosphatase is, within limits, a measure of molecular size. Fig. 6 indicates results obtained when using the fractions described and also two reference com-

pounds, namely adenylic acid and adenosine-cytosine dinucleotide (a commercial sample supplied by B.D.H. Ltd.). While the measurements were being made, no inorganic phosphate was liberated from deoxyribonucleic acid. From Fig. 6 it is seen that most of the polynucleotide fragments have a mean molecular weight considerably greater than that of the dinucleotide. The relative positions of the curves agree with the results obtained by viscosity measurements.

(f) *Further action of deoxyribonuclease.* Recent evidence (Chargaff and Zamenhof, *J. Biol. Chem.*, 1949, **178**, 531) indicates the existence of an enzyme-resistant core in deoxyribonucleic acid which does not dialyse. Our non-dialysable fraction (S_1) was converted by deoxyribonuclease into a readily dialysable fraction S_{1A} (27·5%, if experimental loses are neglected) and a non-dialysable fraction S_{1B}. In agreement with Zamenhof and Chargaff (*loc. cit.*) the non-dialysable fraction (S_{1B}) was completely resistant to the further action of deoxyribonuclease. From Fig. 6 it is clear that the fractions S_{1A} and S_{1B} differ considerably in molecular size. The fact that S_{1A} was dephosphorylated to the extent of 75% by the prostate phosphatase, whereas an authentic mononucleotide and dinucleotide were dephosphorylated to the extent of 100% and 60% respectively, suggested that S_{1A} contained some mononucleotides. This was confirmed by dephosphorylating fraction S_{1A} with prostate phosphatase and separating the products on a paper chromatogram. The positions of the products on the chromatogram were determined by the method of Hotchkiss (*J. Biol. Chem.*, 1948, **175**, 315). [Control experiments showed that nucleotides, *i.e.*, adenylic acid, adenosine–cytosine dinucleotide, or S_{1A}, did not move on the chromatogram, under the conditions used.] Two products were recognised with absorption max. at 266—267 and 258 mμ. (R_F values, 0·42 and 0·67) respectively. A comparison of these absorption maxima with the values previously recorded for the purines and pyrimidines and their corresponding deoxyribosides (Heyroth and Loofbourow, *J. Amer. Chem. Soc.*, 1931, **53**, 3441; Stimson and Reuter, *ibid.*, 1945, **67**, 847, 2191; Hotchkiss, *loc. cit.*) suggested the presence of thymine deoxyriboside, but did not completely identify the nucleosides.

Since chromatography of larger quantities of the initial enzyme digest failed to give a sharp separation of the components, the corresponding products from three chromatograms were combined and then hydrolysed with sulphuric acid at 175° for 2·5 hours in order to liberate the free bases. After neutralisation neither of the hydrolysates gave a precipitate with silver nitrate, but after appropriate treatment the solution of the base separated from the component with absorption max. at 258 mμ. gave a positive reaction for thymine [Hunter's method (*Biochem. J.*, 1936, **30**, 745), as adapted to microquantities by Woodhouse (*Biochem. J.*, 1949, **44**, 185)]. Since no purines were precipitated as silver complexes at pH 6 (cf. Gulland *et al.*, *loc. cit.*) it would appear that the second nucleoside (absorption max. 266—267 mμ.) is cytosine deoxyriboside. Confirmation of this should be possible by the recent method of Cohn (*Science*, 1949, **109**, 377) in which relatively large quantities of purines, pyrimidines, and nucleosides may be separated by ion-exchange resins. This is being investigated.

The presence of mononucleotides among the products of the enzymic degradation was only demonstrated by the above method in fraction S_{1A}; the components of fractions S_2, W_7 (see p. 2753), and O_2 after treatment with prostate phosphatase failed to move from the initial spot on the paper chromatogram.

(g) *Purine : pyrimidine ratios.* Fractions S_2, S_3, and S_{1B} were hydrolysed with sulphuric acid for 2 hours at 175° and the constituent purines and pyrimidines separated by precipitation as silver complexes (Gulland *et al.*, *loc. cit.*). Nitrogen analyses (micro-Kjeldahl) gave the following values for the ratio of purine-N : pyrimidine-N: S_2 0·44, S_3 0·46, S_{1B} 2·37. These values indicate an increased ratio of pyrimidines to purines in the readily dialysable products (S_2 and S_3), whereas the non-dialysable fraction (S_{1B}) which resists further action of the enzyme contains an increased ratio of purines to pyrimidines.

Discussion.—This work shows that in contrast to the conclusions of Fischer *et al.* (*loc. cit.*) the polynucleotides resulting from the enzymic degradation of deoxyribonucleic acid are not homogeneous tetranucleotides, but exhibit a wide range of molecular size. They appear to range from about tri- or tetra-nucleotides to a relatively large fragment which fails to dialyse in the absence of salts. Although mononucleotides are not normally encountered among the products of the enzymic degradation (cf. Klein, *loc. cit.*), subsequent action of the enzyme on the large fragment liberates some pyrimidine mononucleotides. This observation, coupled with the fact that the smaller, readily diffusible products of the enzyme action contain an increased ratio of pyrimidines to purines compared with the native nucleic acid, indicates that deoxyribonuclease preferentially hydrolyses the pyrimidine nucleotide groupings of the deoxyribonucleic acid molecule.

From the foregoing account it follows that the action of deoxyribonuclease on deoxyribonucleic acid is closely analogous to that of ribonuclease on ribonucleic acid. The latter action is known from micro-dilalometric measurements to involve an initial depolymerisation of the nucleic acid into smaller units (Chantrene, Linderstrøm-Lang, and Vanderdriesche, *Nature*, **1947**, **159**, 877) which are then hydrolysed to lower polynucleotides of varying molecular size (Schmidt, Cubilees, Schwartz, and Thannhauser, *J. Biol. Chem.*, **1947**, **170**, 759). Furthermore it is apparent from the work of Schmidt *et al.* (*loc. cit.*) and of Loring, Carpenter, and Roll (*ibid.*, **1947**, **169**, 601) that ribonuclease preferentially hydrolyses the pyrimidine nucleotide groups of the ribonucleic acid molecule and leaves a non-diffusible core, which contains an increased ratio of purines to pyrimidines and is resistant to further action of the enzyme.

The fact that both ribonuclease and deoxyribonuclease preferentially hydrolyse the pyrimidine nucleotide groupings of the corresponding nucleic acid may, as discussed elsewhere (Overend and Webb, *Research*, **1950**, **3**, 238), have some bearing on the specificity of these enzymes.

Experimental.

Preparation of Deoxyribonuclease.—Deoxyribonuclease was isolated from ox-pancreas (20 lbs.) according to McCarty's method (*J. Gen. Physiol.*, **1946**, **29**, 123). The final precipitate obtained after repeated fractional precipitation with ammonium sulphate was collected with suction on hardened filter paper (Whatman No. 54) after 24 hours, redissolved in distilled water (15 c.c.), and dialysed at 1° against frequent changes of 0·002N-sulphuric acid until free from salts. The remaining solution was dried in the frozen state to give a white powder (5 g.) which dissolved readily in water. The enzyme preparation contained no ammonium ions, was free from adenine and guanine deaminase, and was devoid of ribonuclease and nucleotidase or phosphatase activity. It had weak proteolytic activity when examined in 1% (w/v) solution against a casein substrate, but exhibited no hydrolytic activity against Witte peptone. In the Tiselius apparatus, one major electrophoretic component was observed together with a small amount of a second component which had approximately the same mobility.

Some Properties of the Enzyme.—The properties of the enzyme were determined, using both a commercial preparation of thymus sodium deoxyribonucleate (B.D.H. Ltd.) and highly polymerised preparations of deoxyribonucleic acid isolated from calf thymus gland and herring roe according to the method of Mirsky and Pollister (*Proc. Nat. Acad. Sci.*, **1942**, **28**, 344). The analytical data and properties of these preparations will be recorded in a subsequent communication, and the present account refers only to the results obtained with the commercial samples of thymus sodium deoxyribonucleate. The use of the commercial (partly degraded) nucleic acid in these experiments appeared justified, since one of the objects of the present work was the production of polynucleotides of small molecular weight for structural and other investigations.

Since the commercial thymus sodium deoxyribonucleate contained free inorganic phosphate ions and traces of magnesium ions, it (7 g.) was purified by dissolution in the minimum amount of water followed by dialysis for 6 hours against water (4 l.) containing 5N-ammonia solution (2 c.c.). The sodium deoxyribonucleate was recovered by pouring the filtered solution into ethanol (2 l.) containing 0·85% (w/v) sodium chloride solution (50 c.c.). The precipitate was collected by filtration and dried at room temperature. The resulting white powder (4·5 g.) was free from inorganic phosphate and magnesium ions (Found: N : P, 1·6; Purine-N : Pyrimidine-N, 1·57).

A preliminary determination of the activity of the enzyme [1·0 c.c. of a 0·5% (w/v) solution in water containing magnesium sulphate (0·05%)] against 1·0% (w/v) thymus sodium deoxyribonucleate (2·0 c.c.) at pH 7·0 (0·2M-veronal buffer, 1·0 c.c.) showed that the preparation, under these conditions, completely degraded this nucleic acid to acid-soluble material [as shown by the addition of 5N-hydrochloric acid (0·01 c.c.)] within 12 hours at 37° without the liberation of inorganic phosphate.

(a) *Activation by magnesium ions.* Magnesium sulphate solutions (1·0 c.c.) of increasing concentrations were added to a series of tubes each containing a solution of purified sodium deoxyribonucleate (1·0%, w/v; 2·0 c.c.), 0·2M-veronal buffer (pH 7·0; 1·0 c.c.), distilled water (0·5 c.c.), and 1·0% (w/v) deoxyribonuclease in water (0·5 c.c.). The tubes were incubated at 37° for 18 hours, and then an aliquot (4·0 c.c.) of each solution was transferred to a tared centrifuge tube. The acid-insoluble material remaining in each tube was precipitated by the addition, from a pipette, of 5N-hydrochloric acid (2 drops). The precipitates were collected by centrifuging, dehydrated with ethanol, and washed by centrifuging them first with ethanol and then with ether. After being dried *in vacuo* the tubes were re-weighed, and the influence of the magnesium ion on the activity of the enzyme, as measured by the change in weight of the acid-insoluble material, was determined:

Log of molar concn. of Mg^{++} added	−1	−2	−3	−4	−5	−6
% Nucleic acid recovered	3·6	6·6	68	86	92	94

[McCarty (*loc. cit.*) found 0·003M-Mg^{++} to be the optimal concentration for the activation of systems containing varying amounts of enzyme but a fixed amount of nucleic acid.] Control experiments showed that this method of determining enzyme activity was reproducible and that its accuracy was within 5%.

(b) *Optimum* pH *for the activity of deoxyribonuclease.* A series of tubes containing purified sodium deoxyribonucleate (1%; 2 c.c.), 0·1M-magnesium sulphate (1·0 c.c.), distilled water (0·5 c.c.), and deoxyribonuclease solution (0·1%; 0·5 c.c.) were adjusted to the pH values shown below with 0·2M-phosphate

buffers (1·0 c.c.). The tubes were incubated at 37° for 12 hours and the extent of the enzymic hydrolysis was then determined in aliquots of each solution by acid precipitation as described above. (Average values of several determinations are quoted in this and subsequent experiments.)

pH	3·8	4·5	5·9	6·1	7·2	7·9	9·4
Nucleic acid degraded (%)	44	64	78	79	95	94	70

Determination of the Minimum Enzyme Concentration Required for Degradation of the Nucleic Acid Sample.—Solutions of varying enzyme concentrations (0·5 c.c.) were added to a series of tubes containing thymus sodium deoxyribonucleate solution (1%; 2·0 c.c.), 0·1M-veronal buffer (pH 7·0; 1·0 c.c.), 0·1M-magnesium sulphate (1·0 c.c.), and distilled water (0·5 c.c.). After 12 hours at 37°, the acid-precipitable material was determined in the usual way. Results were:

Log of (final) enzyme concn.	−1	−2	−3	−4	−5	−6	−7
Nucleic acid recovered (%)	—	5	5	8	48	82	90

Inactivation of Deoxyribonuclease by Heat.—Solutions of deoxyribonuclease (1%), buffered at pH 7·0, were maintained for 1 hour at the temperatures shown below. After they had cooled to room temperature their activities against thymus sodium deoxyribonucleate at pH 7·0 were determined in the usual way:

Temp. to which enzyme had been heated	50°	60°	70°	80°	90°	100°
Nucleic acid recovered (%)	—	—	5	15	88	92

Determination of the Acid Groups liberated by the Action of Deoxyribonuclease on Thymus Deoxyribonucleic Acid.—An aqueous solution of sodium deoxyribonucleate (96 c.c., containing 0·592 mg. of organic P per c.c.), together with 0·1M-magnesium sulphate (19 c.c.), was adjusted to pH 7·5 (glass electrode) with 0·01N-sodium hydroxide. The solution was diluted (final volume, 120 c.c.) and divided into two equal portions (I & II). To (I) deoxyribonuclease solution [15 c.c.; 0·002% (w/v)] was added, and to (II) the same enzyme solution (15 c.c.) previously inactivated by heating it for 1 hour at 100° was added. Each solution was diluted to 100 c.c. and incubated at 37° for 18 hours (time for completion). Aliquots (10 c.c.) of each solution were then titrated with standard alkali (phenolphthalein). The difference between the mean titres of (I) and (II) (1·268 c.c. of 0·0091N-NaOH) was a measure of the acid groups liberated by the action of deoxyribonuclease, since control experiments in which aliquots (15 c.c.) of the above enzyme solution, adjusted to pH 7·5 and diluted to 100 c.c., were titrated initially and again after 18 hours at 37° showed that no self-hydrolysis of the enzyme, with the liberation of titratable acid groups, occurred under these conditions. The results show that 0·503 acid equivalent per 4 atoms of phosphorus are liberated by the enzymic action.

Variation of Deoxyribonuclease Activity with Time.—A series of tubes, each containing 1% sodium deoxyribonucleate (2·0 c.c.), 0·1M-veronal buffer (pH 8·0; 1·0 c.c.), 0·1M-magnesium sulphate (1·0 c.c.), and 0·001% (w/v) deoxyribonuclease solution (1·0 c.c.), was incubated at 37°. At suitable time intervals, duplicate tubes were withdrawn and the acid-precipitable material was determined in the usual manner. The results are shown in Fig. 1. If the concentration of the enzyme solution was increased to 0·1%, the substrate concentration remaining unchanged, equilibrium was reached in 1·5 hours.

Viscosity determinations were carried out initially at 36° on 2 c.c. of solution in the viscometers described by Koch, Orthmann, and Degenfelder (*J. Amer. Leather Chem. Soc.*, 1939, **34**, 489). The substrate solution used contained 1% sodium deoxyribonucleate (2·0 c.c.), 0·2M-veronal buffer (pH 6·9; 1·0 c.c.), 0·1M-magnesium sulphate (1·0 c.c.), and distilled water (0·5 c.c.). The solution was brought to 36° and a solution of deoxyribonuclease in water (0·002%, 0·5 c.c.) at 36° was added. After thorough mixing, an aliquot (2 c.c.) was transferred to the viscometer. Later experiments were carried out in Ostwald viscometers on 5 c.c. of solution. The buffered substrate solution (4·5 c.c.) described above was introduced into the viscometer supported in a thermostat at 36°, and the temperature allowed to equilibrate. The deoxyribonuclease solution (0·5 c.c. of a 0·002% solution), preheated to 36°, was then added and measurements were commenced immediately after thorough mixing. Results are shown in Fig. 2. After a slight fall in viscosity owing to dilution, no further change occurred in the viscosity of a solution containing 1% sodium deoxyribonucleate (2·0 c.c.) and water (0·5 c.c.), buffered to pH 6·92 with 0·2M-veronal buffer (1·0 c.c.), followed the addition of 0·1M-magnesium sulphate solution (1·0 c.c.), but a rapid decrease in the relative viscosity of the system followed the addition of 0·002% deoxyribonuclease solution (0·5 c.c.) which was free from metallic ions. If the above experiment was carried out with the water (0·5 c.c.) replaced by 0·1N-sodium arsenate (0·5 c.c.) there was no decrease in viscosity. Results are shown in Fig. 3.

Large-scale Hydrolysis of Deoxyribonucleic Acid with Deoxyribonuclease, and Fractionation of the Resulting Degradation Products.—A solution of commercial thymus sodium deoxyribonucleate (B.D.H. Ltd.; ash, 14%; moisture, 26·5%) (100 g.) in water (2 l.) and 0·2M-magnesium sulphate (125 c.c.) was buffered with 0·2M-veronal buffer (pH 7·0; 625 c.c.) and incubated for 30 hours at 37° with deoxyribonuclease (0·4 g.). The solution was maintained at neutral pH by the addition of 0·1N-sodium hydroxide at suitable intervals. During the hydrolysis a sticky solid separated which adhered to the walls of the containing vessel and was isolated by decantation of the clear supernatant solution. After being dried with ethanol and ether, this residual solid (10 g.) gave the usual protein reactions, was soluble in dilute acids, but was sparingly soluble in dilute sodium hydroxide solution. It gave a weak Molisch reaction and appeared to consist mainly of a basic protein derived from the commercial sample of deoxyribonucleic acid. It was therefore discarded.

The supernatant solution containing the degradation products of the deoxyribonucleic acid was concentrated by pervaporation at room temperature to 750 c.c. During this procedure, veronal crystal-

lised both in the solution and on the outer surface of the cellophane sac; the polynucleotides, however, remained in solution and did not diffuse through the membrane during the evaporation. The concentrated solution was adjusted to pH 2·9 with 5N-hydrochloric acid and clarified by filtration. The filtrate was made slightly alkaline (pH 8) with N-sodium hydroxide, and the precipitate of magnesium hydroxide collected at the centrifuge. This precipitate contained some organic (polynucleotide) material which was recovered by solution in 0·25N-hydrochloric acid and re-precipitated with MacFadyen's reagent (uranyl acetate in trichloroacetic acid) (*J. Biol. Chem.*, 1934, **107**, 299). The precipitate was dissolved in 0·1M-sodium carbonate (2 c.c.) and diluted with water (10 c.c.), and ethanol (36 c.c.) was added. The solid which separated was dehydrated with ethanol and after being dried with ethanol and ether was obtained as a white powder (0·67 g.).

A preliminary fractionation of the above solution (pH 8), containing the main bulk of the mixed polynucleotides, was attempted by dialysis against distilled water (3 l.) for 3 days at 0°. The solution remaining inside the cellophane sac was then added to ethanol (2 vols.), and the resulting precipitate (6·6 g.; fraction R) dried with ethanol and ether. The dialysate (3 l.) was concentrated under diminished pressure at 40° to 750 c.c. and then precipitated with uranyl acetate in trichloroacetic acid (MacFadyen, *loc. cit.*). The precipitate was collected at the centrifuge and redissolved in 0·1M-sodium carbonate (200 c.c.), and the solution added to absolute ethanol (5 vols.). The mixture of polynucleotides precipitated was dehydrated with ethanol and ether, to yield a pale yellow powder (38 g.; fraction S). From evidence obtained later it was apparent that dialysis under the conditions above effected little if any separation of the polynucleotides and merely distributed them into the two fractions S and R of essentially similar composition.

Partial Fractionation of Fraction S.—(a) *Dialysis of mixed polynucleotides* (S). A solution of S (5 g.) in distilled water (200 c.c.) was dialysed at 1° against distilled water (3 l.) changed at intervals. Each dialysate was evaporated under diminished pressure at 40° to 50 c.c. and then added to ethanol (250 c.c.). The resulting precipitate was collected at the centrifuge after 12 hours, washed with ethanol, and dried with ethanol and ether. Dialysis was continued until the final dialysate after concentration afforded no precipitate when added to ethanol. In this way, seven fractions, including the non-dialysable fraction S_7, were collected. S_1 and S_2 were both obtained after 3 days. S_1 was an inorganic fraction

Time of dialysis (days)	3	6	9	13	17	—
Fraction	S_1 & S_2	S_3	S_4	S_5	S_6	S_7 (residue)
Weight (g.)	0·052 & 1·92	0·49	0·23	0·13	0·02	0·35

which crystallised from the concentrated dialysate. S_2 and S_3 were readily soluble in water, dilute acids, and sodium hydroxide. S_3 was soluble in water and acids. Dilute solutions were completely precipitated by molybdate in acid solution. S_7 was a non-dialysable residue, soluble in water; aqueous solutions, in contrast to fractions S_1—S_6, frothed readily on shaking, and gave a slight precipitate with acetic acid; ammonium molybdate in acid solution gave a copious precipitate.

Some further fractionation of S_3 (0·82 g.) was obtained by adjusting its solution in water (20 c.c.) to pH 4 with 5N-acetic acid and adding 10% ammonium molybdate (6 c.c.). The precipitate formed was removed (centrifuge) and the supernatant liquor treated with 10N-acetic acid (3 c.c.). A further precipitate separated. The precipitates (fraction M; 0·47 g.) were combined, washed with N-acetic acid containing 1% ammonium molybdate, and dried with ethanol and ether. The addition of both ammonium molybdate and acetic acid to the supernatant solution failed to produce further precipitation, but the addition of 0·25% uranyl acetate in 2·5% trichloroacetic acid (10 c.c.) precipitated further polynucleotide material (0·46 g., after drying with ethanol and ether) since the precipitate gave a positive test for deoxyribose with the Dische diphenylamine reagent.

(b) *Controlled precipitation with ethanol.* The direct addition of increasing amounts of ethanol to a solution of S (10 g.) in water (100 c.c.) initially gave precipitates which contained little polynucleotide material and were mainly inorganic in nature. After complete removal of the inorganic fractions by the total addition of 225 c.c. of ethanol, no further precipitation occurred until the ethanol concentration reached 80%; fraction W_1 (0·35 g.) was then obtained. The volume of the solution at this stage was such that further fractionation could not be conveniently achieved. Accordingly a solution of S (20 g.) in water (200 c.c.) was added to ethanol (400 c.c.), and the resulting precipitate removed by filtration. The filtrate was concentrated at 40° (bath-temp.) to 70 c.c. and an equal volume of ethanol added. The precipitate (O_1; 0·35 g.) which slowly separated was centrifuged off, washed with ethanol, and dried with ethanol and ether. The precipitate (O_2; 1·6 g.) which separated on addition of ethanol (70 c.c.) to the supernatant liquid was collected after 18 hours and dried as above. Repetition of this procedure yielded fractions O_3 (0·1 g.) and O_4 (0·75 g.). Fraction O_5 (0·05 g.) was obtained by the addition of excess of ethanol (6 vols.) to the supernatant liquid remaining after the isolation of O_4.

Diffusion Measurements on the Degradation Products.—The experiments were carried out in the apparatus described by Gage (*Trans. Faraday Soc.*, 1948, **44**, 253) with filter paper (Whatman No. 54) as the diffusion membrane. A solution (0·5%, w/v) of the given fraction (8·0 c.c.) was introduced into the cell, and diffusion allowed to proceed for 17 hours at 36° against distilled water (1·25 l.). The initial solution used and the solution remaining in the cell were then analysed for organic phosphorus by Allen's method (*Biochem. J.*, 1940, **34**, 858), and the percentage diffusion determined. (A control experiment was made using adenylic acid.)

Fraction	Control (adenylic acid)	S_3	S_5	S_7	S_{7B}	R	O_1	O_3	O_4
Mean diffusion (%)	93·4	43·0	20·4	*ca.* 5·0	64	79·1	86·6	86·9	58·6

Action of Prostate Phosphatase on the Fractionated Degradation Products.—The acid phosphatase was isolated from surgically enucleated human prostate glands by essentially the method of Kutscher and Wolbergs (*Z. physiol. Chem.*, 1935, **236**, 237). The minced glands were suspended in water (4 vols.) and allowed to autolyse under toluene for 4 days at 37°. The suspension was then centrifuged and the acid phosphatase removed from the clear supernatant liquid by adsorption on Cy alumina [≈20 mg. of $Al(OH)_3$]. The adsorbent was collected (centrifuge) after 10 minutes and washed with water, and the enzyme eluted with 0·5*M*-citrate buffer (pH 5·6; 2 × 5 c.c.). The combined eluates were saturated with ammonium sulphate, and the resulting precipitate was collected (centrifuge) after 8 hours and dissolved in water (10 c.c.). The solution was dialysed for 70 hours against running tap-water and then dried in the frozen state. A series of tubes, each containing a solution (2%, w/v; 2·0 ml.) of the polynucleotide fraction, 0·2*M*-acetate buffer (pH 5·0; 1·0 c.c.), and a 0·02% (w/v) solution of prostate phosphatase (1·0 c.c.), was incubated at 37°. At suitable intervals, the contents of one tube were precipitated with MacFadyen's reagent (*J. Biol. Chem.*, 1934, **107**, 299) (4·0 c.c.), and the inorganic phosphate was determined colorimetrically in an aliquot (4·0 c.c.) of the filtrate by Allen's method (*loc. cit.*). The results obtained with the polynucleotide fragments and two reference compounds (adenylic acid and adenosine-cytosine dinucleotide) are shown in Fig. 6.

Further Action of Deoxyribonuclease on S_1.—A solution of S_1 (0·22 g.) in distilled water (20 c.c.) was added to a mixture of 0·1*M*-magnesium sulphate (5·0 c.c.), 0·2*M*-veronal buffer (pH 7·6; 10 c.c.), and a 0·002% (w/v) solution of deoxyribonuclease (10 c.c.). After 24 hours at 37°, an aliquot of the digest (40 c.c.) was dialysed at 2° against frequent changes of distilled water until a sample of the dialysate left no residue on evaporation (72 hours). The combined dialysates were concentrated at 40° (bath-temp.) to 30 c.c. and absolute ethanol (4 vols.) was added. The precipitate (S_{1A}) which separated was collected in a tared centrifuge tube, washed with ethanol, and dried with ethanol and ether, to give a white powder (0·065 g.) which contained magnesium sulphate (0·021 g.). The solution remaining in the dialysis sac was added to ethanol (4 vols.), and the precipitate (S_{1B}; 0·095 g.) isolated as above. Thus losses incurred during the experiment being neglected, *ca.* 27·5% of S_1 was rendered dialysable by the further action of deoxyribonuclease. S_{1B} was completely resistant.

Identification of Mononucleotides in Fraction S_{1A}.—The experimental procedure finally adopted was as follows. Fraction S_{1A} (10 mg.) was dissolved in 0·1*M*-acetate buffer (pH 5·0; 3·0 c.c.), and 1·0 c.c. of this solution diluted with distilled water so that the concentration of S_{1A} was 500 μg./c.c. The remaining 2·0 c.c. of the solution were incubated at 37° for 5 hours with a solution of prostate phosphatase (0·02%, w/v; 0·5 c.c.) and then similarly diluted. Some of each solution (0·1 c.c. ≈50 μg. of S_{1A}) was deposited in lanes (2-cm. wide) on a strip (12 × 40 cm.) of Whatman No. 1 filter paper according to the method described by Hotchkiss (*J. Biol. Chem.*, 1948, **175**, 315). The chromatogram was run with *n*-butanol saturated with water, as solvent, in an atmosphere of butanol, water, and ammonia (cf. Hotchkiss, *loc. cit.*). After 18 hours at 20° the position of the solvent front was marked, and the paper strip inverted and dried initially at room temperature and then in an oven at 110° for 20 minutes. The position of the nucleosides on the chromatogram could not be developed by any of the methods used to demonstrate the free purines and pyrimidines (Vischer and Chargaff, *J. Biol. Chem.*, 1948, **176**, 705, 715). Accordingly the individual lanes were cut into sections which were then cut into small pieces and separately extracted with water (4·0 c.c.). After the paper pulp had been centrifuged off, the clear supernatant solutions were examined in the Beckman photoelectric quartz spectrophotometer. No material which absorbed ultra-violet light was demonstrated in the eluates from the control runs of S_{1A} alone. In the case of S_{1A} treated with prostate phosphatase, the presence in the eluates of two absorbing substances with maximum absorption at 266—267 and 258 mμ. was demonstrated at R_F values of 0·42 and 0·67. In order to characterise further the nucleoside fractions separated above, the eluates from three chromatograms which exhibited the same absorption maxima were combined. The resulting solutions (absorption max., 266—267 and 258 mμ. respectively) were evaporated to small volume (2—3 c.c.) and hydrolysed with concentrated sulphuric acid (0·4 c.c.) in sealed tubes at 175° for 2·5 hours. According to the method of Woodhouse (*Biochem. J.*, 1949, **44**, 185), the acid solutions were then brought to pH 9 by the addition of hot saturated barium hydroxide solution and filtered from the precipitated barium sulphate. After evaporation the solutions (5—10 c.c.) were acidified to pH 6 with 5*N*-nitric acid, and 5% silver nitrate (1 c.c.) was added to each. As in each case, no precipitate was formed (absence of purines), the solutions were made alkaline to pH 9 with barium hydroxide solution and the resulting precipitates collected (centrifuge) after 18 hours. These were suspended separately in *N*-hydrochloric acid (3 c.c.), and the suspensions heated at 80° for 30 minutes. After centrifugation, the clear supernatant solutions were neutralised with sodium carbonate and tested for the presence of thymine by Hunter's method (*Biochem. J.*, 1936, **30**, 745) as adapted to micro-quantities by Woodhouse (*loc. cit.*). A positive reaction was given by the solution of the base separated from the nucleoside fraction with absorption maximum at 258-mμ.

The authors thank Professor M. Stacey, F.R.S., for his interest and encouragement, Mr. S. Laland for help with the analyses, and the British Empire Cancer Campaign (Birmingham Branch) for financial support.

CHEMISTRY DEPARTMENT,
THE UNIVERSITY, BIRMINGHAM 15.

[*Received, May 3rd*, 1950.]

529. *The Reaction of Diborane with Some Alkene Oxides and Vinyl Compounds.*

By F. G. A. Stone and H. J. Emeléus.

Diborane reacted rapidly with ethylene oxide at −80° forming diethoxyborine and a solid polymer containing *ca.* eight oxide units per molecule. Propylene oxide reacted similarly, forming di*iso*propoxyborine and a liquid polymer containing *ca.* six oxide units per molecule. Both polymers contained boron, and were shown to be of the type $H{\cdot}[CHR{\cdot}CH_2O]_x{\cdot}BH_2$. The reaction between boron trifluoride and ethylene oxide was studied under similar conditions. The mechanism of the reactions is discussed. Preliminary experiments showed that reactions of diborane with acrylonitrile, methyl methacrylate, and styrene were complex. The main product in each case appeared to be a trialkyl derivative of boron.

The electron-deficient nature of the so-called borine molecule is well known and its co-ordinating power is one of the characteristic features of diborane chemistry (Burg and Schlesinger, *J. Amer. Chem. Soc.*, 1937, **59**, 780). The reactions described below were studied in order to investigate the effect of diborane on molecules where co-ordination might be followed by molecular rearrangement, leading to further reaction, or where the transient existence of the borine molecule might initiate a reaction.

Diborane reacted rapidly with ethylene oxide and propylene oxide at −80°. At room temperature, in the gas phase, the reaction proceeded more slowly. From ethylene oxide, diethoxyborine was formed, together with a white polymeric solid. The latter contained, on the average, eight oxide units per molecule. Propylene oxide reacted in a similar manner, the products being di*iso*propoxyborine and a liquid polymer with an average of six oxide units per molecule. The polymers obtained from both alkene oxides contained boron. Infra-red analysis of these polymers has shown that they do not contain hydroxyl groups or olefinic double bonds. The infra-red spectra do, however, show the presence of B–H stretching frequencies identical with those of the terminal BH_2 groups in diborane (Stitt and Price, *J. Chem. Physics*, 1941, **9**, 780; 1947, **15**, 614). The spectrum of the polymer from ethylene oxide also shows an absorption band characteristic of a methyl group.

There is evidence, therefore, that the structure of the polymers is of the type $H{\cdot}[CHR{\cdot}CH_2{\cdot}O]_x{\cdot}BH_2$, where R = H or CH_3 according to whether the polymer is derived from ethylene or propylene oxide. The wax-like polymer from ethylene oxide has a melting range of from 45° to 50° and, like its analogue derived from propylene oxide, is hygroscopic, insoluble in ether, and soluble in water or alcohol with the evolution of a small quantity of hydrogen. Depolymerisation occurs when the polymers are heated under a high vacuum.

Observations on the dialkoxyborines, produced simultaneously with the polymers, have confirmed those made by Brown, Schlesinger, and Burg (*J. Amer. Chem. Soc.*, 1939, **61**, 673).

In order to correlate the reactivity of the borine molecule with that of boron trifluoride, a reaction between ethylene oxide and boron trifluoride at −80° was carried out in the high-vacuum apparatus, under the same conditions as were used for diborane.

Such a reaction is also of interest in the study of boron trifluoride-catalysed polymerisations in general, since, under the conditions used, any hydroxylic co-catalyst would be rigidly excluded. The presence of water vapour or other compounds containing a hydroxyl group has been shown to be necessary for the polymerisation of *iso*butene by boron trifluoride (Evans and Meadows, *J. Polymer Sci.*, 1949, **4**, 359; Symposium on Friedel–Crafts Catalysts, *Nature*, 1949, **164**, 655). It is possible, however, that in the reaction between boron trifluoride and ethylene oxide the latter itself acts as a co-catalyst. The reaction is highly exothermic; dioxan is formed together with liquid polymeric boron-containing material, which readily depolymerises at room temperature to give dioxan and less volatile material. A preliminary study of the infra-red spectra of the polymer has shown the absence of any absorption due to an olefinic double bond or hydroxyl group.

The action of the boron trifluoride–ether complex on cyclic oxides in the presence of compounds containing a carbonyl group has been studied by Petrov (*J. Gen. Chem. Russia*, 1940, **10**, 981; 1944, **14**, 1038; 1946, **16**, 61), who found that considerable polymerisation of the oxides occurred as a side reaction even in the presence of a solvent. It is probable that the reaction between diborane and the cyclic oxides involves the intermediate formation of a borine complex, in which the boron atom of the borine molecule is co-ordinated to the oxygen atom of the oxide. This hypothesis is based on the recognised reactions of diborane with ethers, aldehydes, and ketones at −80° (Schlesinger and Burg, *J. Amer. Chem. Soc.*, 1938, **60**, 290; Brown, Schlesinger, and Burg, *ibid.*, 1939, **61**, 673). The formation of the dialkoxyborines by

the action of diborane on the alkene oxides is of particular interest, since these compounds are also formed by the reaction of diborane with aldehydes and ketones. Indeed, a mechanism can be postulated to explain the formation of the dialkoxyborines from the alkene oxides similar to that suggested by Brown, Schlesinger, and Burg to explain their production from aldehydes and ketones. The mechanism suggested by the latter workers, taking acetaldehyde as the example, was :

$$CH_3{\cdot}CHO + BH_3 \longrightarrow \underset{(A)}{CH_3{\cdot}CHO{:}BH_3} \longrightarrow \underset{(B)}{CH_3{\cdot}CH_2{\cdot}O{\cdot}BH_2} \xrightarrow{CH_3{\cdot}CHO} (CH_3{\cdot}CH_2{\cdot}O)_3BH$$

Similarly for ethylene oxide, we have

$$BH_3 + \underset{\diagdown O \diagup}{CH_2{-}CH_2} \longrightarrow \underset{\substack{\diagdown O \diagup \\ \vert \\ BH_3 \\ (A)}}{CH_2{-}CH_2} \longrightarrow \underset{(B)}{CH_3{\cdot}CH_2{\cdot}O{\cdot}BH_2} \xrightarrow[(CH_2)_2O]{} (CH_3{\cdot}CH_2{\cdot}O)_3BH$$

Thus the action of diborane on both acetaldehyde and the isomeric ethylene oxide probably results in the formation of the monoalkoxyborine (*B*) which undergoes further reaction to give diethoxyborine. In both cases the step from (*A*) to (*B*) involves the transfer of a proton with a pair of electrons. In the case of the ethylene oxide–borine complex the breaking of the cyclic ring also takes place. The ethylene oxide molecule itself is subject to a considerable amount of internal strain, and it is likely that its borine complex is also unstable. This step would therefore require little energy.

It is possible for the borine–ethylene oxide complex to undergo ring fission without the transfer of a proton with a pair of electrons, and this would lead to the formation of the initiating unit $\overset{+}{C}H_2{\cdot}CH_2{\cdot}O{\cdot}\bar{B}H_3$ and to the possibility of polymerisation by reaction with further ethylene oxide molecules. In order to achieve a neutral polymer molecule a chain termination of four steps is necessary. The evidence from the infra-red spectra that there is no double bond in the polymer molecule, together with the absence of the formation of significant amounts of hydrogen gas, excludes chain termination by the reaction :

$$\bar{B}H_3{\cdot}[O{\cdot}CH_2{\cdot}CH_2]_n{\cdot}O{\cdot}CH_2{\cdot}\overset{+}{C}H_2 + \bar{B}H_3{\cdot}[O{\cdot}CH_2{\cdot}CH_2]_n{\cdot}O{\cdot}CH_2{\cdot}\overset{+}{C}H_2 \longrightarrow$$
$$\bar{B}H_3{\cdot}[O{\cdot}CH_2{\cdot}CH_2]_n{\cdot}O{\cdot}CH{=}CH_2 + H_2 + BH_3[O{\cdot}CH_2{\cdot}CH_2]_n{\cdot}O{\cdot}CH_2{\cdot}\overset{+}{C}H_2$$

Any suggested mechanism for the polymerisation of alkene oxides by diborane must, however, await final confirmation from a study of the kinetics, in particular the effect of temperature change, diborane concentration, and monomer concentration.

Polymerisation reactions induced by diborane are not unknown. Brown, Schlesinger, and Burg report the formation of large amounts of paraldehyde together with a polymer of monoalkoxyborine $(CH_3{\cdot}CH_2{\cdot}O{\cdot}BH_2)_x$ in the reaction of diborane and acetaldehyde (*loc. cit.*). Hydrocarbons such as methane react with diborane at about 100°, and paraffin-chain synthesis and the formation of boron–carbon bonds occurs (Hurd, *J. Amer. Chem. Soc.*, 1948, **70**, 2053).

These reactions suggested that diborane might polymerise vinyl compounds. It was found that acrylonitrile, methyl methacrylate, and styrene reacted slowly with diborane at room temperature. The main product in each case appeared to be a trialkyl derivative of boron. The action of diborane on vinyl compounds thus appears to be parallel to that of diborane on olefins, a reaction which also gives boron trialkyls (*idem*, *ibid.*), *viz.*

$$B_2H_6 + 6R{\cdot}CH{=}CH_2 = 2(R{\cdot}CH_2{\cdot}CH_2)_3B$$

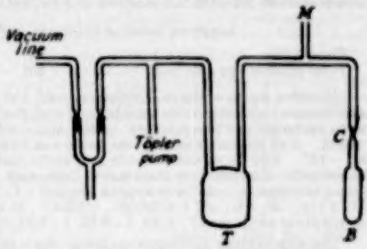
For the reactions between diborane and styrene, and diborane and methyl methacrylate, the reaction ratio of diborane to vinyl compound was close to 1 : 6. Acrylonitrile and diborane, however, reacted to give at least three products, and the ratio of reactants varied considerably with each experiment as the proportion of the products changed. All the latter were non-volatile *in vacuo* even at temperatures as high as 70°. The main product was a red solid, insoluble in all common solvents, but which could be hydrolysed by boiling hydrochloric acid to give its boron content as boric acid. A pale yellow solid was also formed together with a non-volatile oil. Mixtures of products are highly probable because of the possibility of co-ordination of borine molecules to any nitrogen atom capable of donating a pair of electrons. The reaction products deserve further study.

The products from styrene and methyl methacrylate were viscous liquids easily oxidised by air, that from styrene being oxidised with the evolution of a considerable amount of heat.

Experimental.

Apparatus and Technique.—The experimental work was carried out in a high-vacuum apparatus of the type used by Stock and his co-workers (Stock, "Hydrides of Boron and Silicon," Cornell Univ. Press; *Ber.*, 1921, **54**, 142). The reaction vessel is shown in the figure. A small bulb *B*, fitted with a capillary *C*, was attached to the vacuum line by means of a Stock valve. The manometer *M* allowed pressure changes to be followed, and the U-trap *T* was used to condense volatile compounds of the reaction before any non-condensable gas was taken off with the Töpler pump. A known weight of the organic compound was distilled into *B*, followed by a known volume of diborane. The Dewar flask of liquid nitrogen surrounding *B* was then removed, and the diborane allowed to vaporise and react with the organic liquid. In the case of the cyclic oxides, the bulb was cooled in a solid carbon dioxide–alcohol bath during the experiment. At the end of a reaction, after any non-condensable gas had been removed by the Töpler pump, unreacted diborane and organic compound, together with any volatile products, were taken into the vacuum apparatus for separation by trap-to-trap distillation and fractional condensation. Any non-volatile reaction product formed in *B* could be removed for analysis by sealing off the capillary.

The diborane used in the experiments was prepared by reduction of boron trichloride with lithium aluminium hydride (Finholt, Bond, and Schlesinger, *J. Amer. Chem. Soc.*, 1947, **69**, 1199). Boron trifluoride, obtained from a commercial cylinder, was purified by distillation in the high-vacuum system. The organic compounds, also obtained commercially, were purified in a similar manner.



All boron analyses were carried out by titration of boric acid in the presence of mannitol.

Reaction between Diborane and the Alkene Oxides.—In a typical experiment 29·8 millimoles of ethylene oxide (Found: *M*, 44·4) were treated with 3·68 millimoles of diborane (v. p. 158 mm. at −117°) at −80°. After 20 hours the volatile compounds in the reaction vessel were removed and separated by distillation. 3·4 Millimoles of ethylene oxide (Found: C, 54·5; H, 9·1%; *M*, 44·5. Calc. for C_2H_4O: C, 54·6; H, 9·1%; *M*, 44) were condensed at −123° and 0·43 millimole of diborane (v. p., 166 mm. at −116°) were trapped at −196°. 3·25 Millimoles of diborane and 26·4 millimoles of ethylene oxide had, therefore, reacted, giving a ratio of reactants B_2H_6 : $(CH_2)_2O$ of 1 : 8·14. Besides the unreacted diborane and ethylene oxide, 0·416 g. of a volatile liquid was condensed at −65° and 0·681 g. of a non-volatile white solid remained in the reaction bulb.

The volatile liquid trapped at −65° was diethoxyborine [Found: B, 10·6, 10·8%; *M*, 100, 102; v. p. 35·5 mm. at 0°. Calc. for $(C_2H_5O)_2BH$: B, 10·6%; *M*, 101·9; lit. value for v. p. at 0°, 37·5 mm. (Brown, Schlesinger, and Burg, *loc. cit.*)]. As reported by the latter workers diethoxyborine decomposes above 0° to give diborane and ethyl borate. The diethoxyborine was kept at room temperature for a week; it was then fractionated to give diborane, diethoxyborine, and ethyl borate [Found: C, 50·0; H, 10·7; B, 7·4, 7·6%;. Calc. for $(C_2H_5O)_3B$: C, 49·4; H, 10·3; B, 7·4%], n_D^{20} 1·3798 (lit., 1·3808).

The *polymer* in the reaction bulb was found to have an average composition corresponding to eight $\cdot CH_2 \cdot CH_2 \cdot O \cdot$ units per molecule of borine, *viz.*, $H \cdot [CH_2 \cdot CH_2 \cdot O]_8 \cdot BH_3$ [Found: C, 51·3, 53·1; H, 9·8, 9·5; B, 2·1, 2·5%; *M* (Rast), 373. $H \cdot [CH_2 \cdot CH_2 \cdot O]_8 \cdot BH_3$ requires C, 52·5; H, 9·6; B, 2·9%; *M*, 366]. It was hygroscopic. A specimen exposed to the atmosphere for one hour before analysis was found to have C, 47·3; H, 8·8%. $H \cdot [CH_2 \cdot CH_2 \cdot O]_8 \cdot B(OH)_2$ requires C, 48·2; H, 8·8%.

Other experiments with diborane and ethylene oxide were carried out, and the ratio of reactants, together with the approximate yields of product, are shown in the following table. In an experiment using excess of diborane the reaction ratio of diborane to ethylene oxide was reduced to 1 : 5·08, and in a vapour-phase reaction the ratio was 1 : 5·35.

B_2H_6 used (millimoles).	$(CH_2)_2O$ used (millimoles).	Ratio.	$BH(OEt)_2$ formed (g.).	Polymer formed (g.).	B_2H_6 used (millimoles).	$(CH_2)_2O$ used (millimoles).	Ratio.	$BH(OEt)_2$ formed (g.).	Polymer formed (g.).
3·28	28·4	1 : 8·66	0·268	0·794	2·13	14·79	1 : 6·95	0·227	0·462
2·26	22·45	1 : 9·94	0·301	0·724	1·68	12·5	1 : 7·45	0·260	0·341

The reaction between diborane and excess of propylene oxide at −80° was similar to that with ethylene oxide. The polymeric material produced was liquid and the diisopropoxyborine formed was characterised by molecular weight, boron analysis [Found: B, 8·35, 8·6%; *M*, 128·3, 130. Calc. for $(C_3H_7O)_2BH$: B, 8·3%; *M*, 129·9], and v. p. at 0° (10·1 mm. Lit. value, *loc. cit.*, 10·0 mm.). After storage for one week at room temperature, it was fractionated to give diborane, a little unchanged dialkoxyborine, and a less volatile liquid [Found, for the last: C, 58·4; H, 11·5; B, 6·05, 5·55. Calc. for $(C_3H_7O)_3B$: C, 57·6; H, 11·2; B, 5·75%].

The liquid *polymer* formed in the reaction was analysed [Found : C, 59·3, 60·9; H, 10·6, 10·6; B, 3·0, 2·9, 2·8%; *M* (Rast), 308, 324. $H{\cdot}[CH(CH_3){\cdot}CH_2{\cdot}O]_6{\cdot}BH_3$ requires C, 59·8; H, 10·8; B, 3·0%: *M*, 362].

Further experimental data for the reaction between diborane and propylene oxide are given below. Diborane used in the reaction was tensimetrically pure. The propylene oxide had C, 61·9; H, 10·1%; *M*, 58·9 (Calc. for C_3H_6O : C, 62·1; H, 10·35%: *M*, 58).

B_2H_6 used (millimoles).	$(CHMe{\cdot}CH_2)O$ used (millimoles).	Ratio.	$BH(OPr)_2$ formed (g.).	Polymer formed (g.).
2·91	14·5	1 : 4·98	—	—
3·79	18·38	1 : 4·85	0·875	0·181
3·34	16·19	1 : 4·85	0·740	0·166
2·88	14·5	1 : 5·03	0·679	0·224

The absorption of diborane by the alkene oxides at −80° proceeds rapidly at first but after an hour the absorption takes place more slowly (see table). The reaction was continued, however, in order to

Reaction between diborane and ethylene oxide at −80°.

Time, hours	0	0·25	0·5	1	2	6	15	20
Pressure of B_2H_6, mm.	208	137	131	126	121	105	86	80·5

increase the yield of products. The rate at which ethylene oxide reacts with diborane in the vapour phase at room temperature is shown in a further table.

Reaction between diborane and ethylene oxide in the vapour phase.

Time, hours	0	0·5	1	1·5	2	2·5	3
Total pressure of gas, mm.	332	326	316	305	297	293	287

Reaction between Boron Trifluoride and Ethylene Oxide at −80°.—In a typical experiment, 22·3 millimoles of ethylene oxide were treated with 3·07 millimoles of boron trifluoride. The reaction appeared to be complete in a few minutes. After an hour the volatile compounds were removed from the reaction vessel. 0·42 Millimole of ethylene oxide was recovered together with 0·159 g. of a volatile liquid trapped at −45°. 0·98 G. of non-volatile polymeric material remained in the trap. No boron trifluoride was recovered. The reaction ratio boron trifluoride to ethylene oxide was, therefore, 1 : 7·1. The volatile liquid trapped at −45° was dioxan (Found : C, 54·5; H, 8·9%; *M*, 88·4. Calc. for $C_4H_8O_2$: C, 54·5; H, 9·1%; *M*, 88); n_D^{25} 1·4226 (lit., 1·4224). In other experiments the reaction ratio of boron trifluoride to ethylene oxide was 1 : 6·46, 1 : 6·23, 1 : 6·23, and 1 : 7·23.

The non-volatile polymeric material was a liquid which depolymerised at room temperature. This depolymerisation was accelerated by gentle warming, under high vacuum, at approximately 40°. The main product of depolymerisation was impure dioxan : *M*, 87·2; n_D^{25} 1·431 (cf. above). A black liquid residue remained in the reaction trap after several hours' pumping and gentle warming (Found : B, 8·8%).

Measurement of the Spectra.—The spectra were measured on a Standard Perkin Elmer Model 12B infra-red spectrometer fitted with a rock-salt prism. Two thicknesses of liquid polymer were used, the thicker layer being 160 μ. and the thinner one 20 μ.

In the case of the solid polymer prepared from ethylene oxide and diborane, a liquid film was produced by gently warming the rock-salt plates of the cell to approximately the m. p. of the polymer before the latter was placed between them. The samples were sealed *in vacuo* for transportation, and the spectra were taken immediately after the samples had been unsealed.

Neither the polymer from ethylene oxide nor that from propylene oxide showed any absorption in the double-bond region 1600—1700 cm.$^{-1}$. There was no absorption band corresponding to a hydroxyl group on freshly opened samples of the polymers, but a sample which had been exposed to the air for a short time showed a weak band at 3300 cm.$^{-1}$.

The polymer from ethylene oxide showed weak absorption bands at 2520 cm.$^{-1}$ and 2620 cm.$^{-1}$, corresponding to the stretching of B-H bonds. These bands were stronger, however, in the lower molecular-weight polymer from propylene oxide. A strong absorption band at 1375 cm.$^{-1}$ in the polymer from ethylene oxide probably indicates a methyl group. A preliminary investigation of the spectra of the polymeric material obtained from boron trifluoride and ethylene oxide also showed no bands at 1600—1700 cm.$^{-1}$ and 3300 cm.$^{-1}$.

Acrylonitrile and Diborane.—In a typical experiment 4·24 millimoles of tensimetrically pure diborane remained in contact with 41·8 millimoles of acrylonitrile for 20 hours at room temperature. All volatile compounds were then removed from the reaction vessel. After fractionation, 1·62 millimoles of diborane and 26·9 millimoles of acrylonitrile were recovered, giving a reaction ratio diborane : acrylonitrile of 1 : 5·7. The solid *product* was analysed (Found : C, 61·9; H, 6·8; N, 23·85; B, 6·6, 6·3. $B_2H_4(CH_2{\cdot}CH{\cdot}CN)_{5\cdot7}$ requires C, 62·1; H, 7·0; N, 24·2; B, 6·55%). In this experiment the product was almost entirely a red solid and there was little formation of yellow solid and oil. In other experiments, however, the proportion of the latter in the reaction product increased. The red and yellow solid reaction products were insoluble in water, alcohol, acetone, ether, chloroform, and benzene, but freely soluble in formodimethylamide.

In other experiments the ratio of reactants diborane : acrylonitrile was 1 : 3·52, 1 : 4·56, 1 : 5·12 The products of this reaction were far more stable in air than those from styrene and methyl methacrylate the latter being rapidly oxidised.

Methyl Methacrylate and Diborane.—In a typical experiment 19·12 millimoles of methyl methacrylate were treated with 4·10 millimoles of diborane. After approximately 20 hours the volatile compounds were taken into the high-vacuum system for separation by distillation : 2·72 millimoles of diborane and 10·47 millimoles of methyl methacrylate were recovered. Thus the ratio of reactants diborane : methyl methacrylate was 1 : 6·26. In a second experiment it was 1 : 5·6. The reaction *product* was a highly viscous liquid, soluble in acetone and benzene. Boron analysis carried out on the products of the two experiments gave B, 3·6 and 3·9% [$[CH_2{\cdot}CH(CH_3){\cdot}CO_2CH_3]_3B$ requires B, 3·45%]. In this preliminary study no evidence for the cleavage of the ester by the borine molecule was observed (Brown, Schlesinger, and Burg, *loc. cit.*).

Styrene and Diborane.—In a typical reaction between excess of styrene and diborane, 0·804 g. of styrene reacted with 0·0207 g. of diborane, giving a ratio of reactants of 6·46 : 1. The *product*, soluble in benzene, had B, 2·7, 3·15% [$(C_6H_5{\cdot}CH_2{\cdot}CH_2)_3B$ requires B, 3·3%].

Rapid oxidation by the atmosphere of the liquid products of the above two reactions prevented accurate values of carbon and hydrogen analysis and molecular weight from being obtained. Values of 260 and 292 were obtained for the two liquids, respectively, by the cryoscopic method, benzene being used as solvent : $[CH_2{\cdot}CH(CH_3){\cdot}CO_2CH_3]_3B$ requires *M*, 314, and $(C_6H_5{\cdot}CH_2{\cdot}CH_2)_3B$ requires *M*, 326.

In the reactions described above diborane was allowed to remain in contact with the organic compounds for approximately 20 hours, small quantities of hydrogen being formed. This gas formation was not connected with the main reaction but was due to a reaction between the surface of the reaction system and the diborane. This was shown by carrying out two blank experiments in which diborane alone was placed in the apparatus for a few hours, during which time 6·2 and 8·9 c.c. of hydrogen were formed. The volume of hydrogen formed in any one experiment depended entirely on the type of pre-treatment given to the glass. In three reactions in which the reaction bulb was merely pumped to a hard vacuum for several hours before an experiment, the volumes of hydrogen formed were 6·85, 6·1, and 7·0 c.c. Before two other experiments the reaction bulb was baked during evacuation ; the volumes of hydrogen formed in these reactions were 4·8 and 5·6 c.c. Formation of hydrogen gas was reduced to a minimum by evacuating the reaction system while heating it and then allowing diborane to remain in the apparatus for a few hours before an experiment. Such pre-treatment of the glass of the system reduced the volume of hydrogen formed in two reactions to 2·8 and 2·88 c.c. All the glass used in the apparatus was subjected to a uniform pre-treatment of washing with chromic acid and distilled water, followed by air-drying.

One of the authors (F. G. A. S.) is indebted to the Department of Scientific and Industrial Research for a Maintenance Grant. The authors also thank Dr. N. Sheppard for photographing and interpreting the infra-red spectra.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, June 3rd*, 1950.]

---

530. *An Unambiguous Synthesis of 3-Aroylflavones and Their Reaction with Benzylamine.*

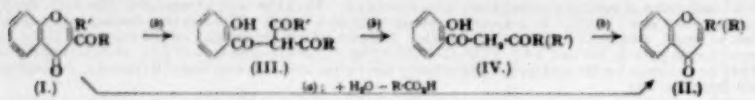
By WILSON BAKER and F. GLOCKLING.

Isomeric pairs of methoxylated 3-aroylflavones (I) and (X) have been prepared from the benzoyl-*o*-hydroxybenzoylmethanes (IV) and (VIII). The latter were condensed with aromatic aldehydes R'·CHO and R·CHO, respectively, to give the arylidene derivatives (VII) and (IX), and these were then oxidised with selenium dioxide to the 3-aroylflavones (I) and (X). Treatment of the 3-aroylflavones, *e.g.*, (X), with benzylamine resulted in all cases in the loss of the 3-aroyl group as an aroylbenzylamide (XII), and formation of an unsaturated benzylamino-compound (XI) ; this general reaction may be used to orient any compound (I) where R and R' are alkyl or aryl groups.

AN *o*-hydroxyacetophenone reacts with the anhydride and the sodium salt of an aliphatic acid to give a 3-acyl-2-alkylchromone (I ; R = R' = alkyl), alkaline hydrolysis of which yields a 2-alkylchromone (II ; R' or R = alkyl) by loss of the acyl group (von Kostanecki *et al.*, *Ber.*, 1901, **34**, 102, 2946). A similar process using the anhydride and the sodium salt of an aromatic acid has been much used for the preparation of flavones (Allan–Robinson synthesis) (II ; R' or R = aryl), and here also the primary product is generally a 3-aroylflavone (I ; R = R' = aryl) (Baker, *J.*, 1933, 1383). The loss of the 3-acyl group may be either direct (*a*) or indirect (*b*), the latter course involving hydrolytic opening of the pyrone ring to give a triacylmethane (III) which passes *via* a diacylmethane (IV) into (II) (for a discussion of the hydrolysis of 3-acyl-chromones and -flavones, see Baker, *loc. cit.* ; Baker and Butt, *J.*, 1949, 2145). Only in the cases of compounds (I) where R and R' are identical would both methods of hydrolysis necessarily give the same product (II).

Intermediates involved in the formation of these 3-acyl compounds (I) have been shown to be the di- and tri-acylmethanes (IV) and (III) (Baker, *loc. cit.* ; Doyle, Gógan, Gowan, Keane, and Wheeler, *Proc. Roy. Dublin Soc.*, 1948, **24**, 291). Hence in the reaction between a diacyl-

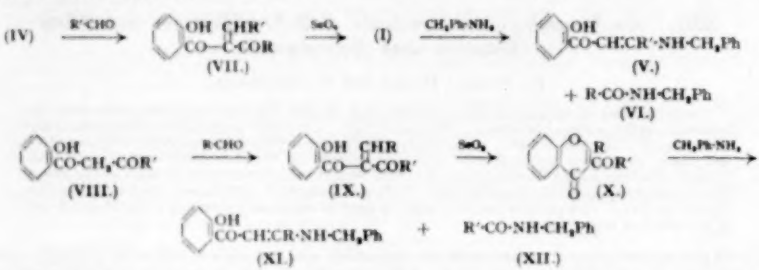
methane (IV) containing the group $\cdot CO \cdot R$ and the anhydride and the sodium salt of an acid $R' \cdot CO_2H$, it is not possible to say whether the product is the 3-acylchromone (I) or its isomeride



(X). Alkaline hydrolysis is unable to distinguish with certainty between two such isomeric structures, because if the pyrone rings open the same 2-alkylchromone might result in each case.

Baker and Butt (*loc. cit.*) showed that 3-acylchromones, *e.g.*, (I), react with benzylamine by removal of the 3-acyl group as an acylbenzylamide and opening of the pyrone ring with formation of yellow fluorescent compounds (V). Thus the acetylation of benzoyl-*o*-hydroxybenzoylmethane (IV; R = Ph) was shown to give 3-benzoyl-2-methylchromone (I; R = Ph, R′ = Me), and not 3-acetylflavone (I; R = Me, R′ = Ph), although alkaline hydrolysis yields flavone (II; R′ = Ph). In order to prove conclusively that reaction with benzylamine proceeded in the way mentioned, it was decided to attempt the unambiguous synthesis of pairs of isomeric 3-acyl compounds, (I) and (X), and then to see if each compound would react with benzylamine in the expected manner. The acylation of a diacylmethane (IV) was clearly inadmissible as a synthetical method, and would in any case probably lead to only one (unoriented) of the desired isomerides, so a new synthetical process had to be devised.

It has now been found possible to make use of Mahal, Rai, and Venkataraman's flavone synthesis (*J.*, 1935, 866; for other references see Adams, "Organic Reactions," 1949, Vol. V, pp. 341, 360 *et seq.*), in which an *o*-hydroxychalkone, *o*-$HO \cdot C_6H_4 \cdot CO \cdot CH{:}CHAr$, is oxidised to a flavone by selenium dioxide, and this has led to the unambiguous preparation of pairs of isomeric 3-aroylflavones, (I) and (X), where R and R′ are different aryl groups. Four such pairs of isomers have been prepared and submitted to reaction with benzylamine; each compound smoothly undergoes the expected cleavage, thus proving the generality of the method for determining the structure of 3-aroylflavones and related compounds. Attempts to apply the selenium dioxide reaction to the synthesis of acylflavones (I; R′ = aryl, R = alkyl) have given anomalous results.



The following synthesis of 3-(3 : 4 : 5-trimethoxybenzoyl)flavone (X; R = Ph, R′ = 3 : 4 : 5-trimethoxyphenyl) is typical of the method used for the preparation of the 3-aroylflavones. *o*-Hydroxyacetophenone was treated with 3 : 4 : 5-trimethoxybenzoyl chloride and pyridine, and the resulting *o*-(3 : 4 : 5-trimethoxybenzoyloxy)acetophenone was converted by molecular rearrangement with potassium hydroxide in anhydrous pyridine into *o*-hydroxybenzoyl-3′ : 4′ : 5′-trimethoxybenzoylmethane (VIII; R′ = 3 : 4 : 5-trimethoxyphenyl) in over 70% yield (Baker–Venkataraman transformation; see Baker, *loc. cit.*; Doyle *et al.*, *loc. cit.*). Reaction of this dibenzoylmethane with benzaldehyde in boiling ethanol in presence of piperidine yielded the benzylidene derivative (IX; R = Ph, R′ = 3 : 4 : 5-trimethoxyphenyl), and reaction of this in boiling *n*-amyl-alcoholic solution with selenium dioxide for 17 hours gave 3-(3 : 4 : 5-trimethoxybenzoyl)flavone (X; R = Ph, R′ = 3 : 4 : 5-trimethoxyphenyl) in 58% yield. The isomeric flavone (I; R = Ph, R′ = 3 : 4 : 5-trimethoxyphenyl) was similarly prepared from 2-benzoyloxyacetophenone *via* benzoyl-*o*-hydroxybenzoylmethane (IV; R = Ph),

ω-benzoyl-ω-o-hydroxybenzoyl-3 : 4 : 5-trimethoxystyrene (VII; R = Ph, R′ = 3 : 4 : 5-trimethoxyphenyl), and final oxidation with selenium dioxide.

Reaction of these isomeric flavones with benzylamine was effected in boiling pyridine solution. 3-(3 : 4 : 5-Trimethoxybenzoyl)flavone gave 3 : 4 : 5-trimethoxybenzobenzylamide (XII; R′ = 3 : 4 : 5-trimethoxyphenyl) and 2-(β-benzylaminocinnamoyl)phenol (XI; R = Ph), while 3-benzoyl-3′ : 4′ : 5′-trimethoxyflavone (I; R = Ph, R′ = 3 : 4 : 5-trimethoxyphenyl) gave benzobenzylamide (VI; R = Ph) and 2-(β-benzylamino-3 : 4 : 5-trimethoxycinnamoyl)-phenol (V; R′ = 3 : 4 : 5-trimethoxyphenyl).

The table names other 3-aroylflavones which have been similarly prepared, and the products obtained by their reaction with benzylamine.

3-Aroylflavones.	Products obtained by reaction with benzylamine.
3-Benzoylflavone	2-β-Benzylaminocinnamoylphenol and benzobenzylamide
3-o-Anisoylflavone	2-β-Benzylaminocinnamoylphenol and *o*-anisobenzylamide
3-Benzoyl-2′-methoxyflavone	2-(β-Benzylamino-2-methoxycinnamoyl)phenol and benzobenzylamide
3-*p*-Anisoylflavone	2-β-Benzylaminocinnamoylphenol and *p*-anisobenzylamide
3-Benzoyl-4′-methoxyflavone	2-(β-Benzylamino-4-methoxycinnamoyl)phenol and benzobenzylamide
3-Veratroylflavone	2-β-Benzylaminocinnamoylphenol and veratrobenzylamide
3-Benzoyl-3′ : 4′-dimethoxyflavone	2-(β-Benzylamino-3 : 4-dimethoxycinnamoyl)phenol and benzobenzylamide
4′-Methoxy-3-veratroylflavone	2-(β-Benzylamino-4-methoxycinnamoyl)phenol and veratrobenzylamide

3-o-Anisoylflavone undergoes demethylation when heated with aqueous hydrobromic acid in acetic acid, giving 3-o-hydroxybenzoylflavone without loss of the 3-aroyl group. This product is an *o*-hydroxy-ketone, and as such might undergo the Dakin oxidation with hydrogen peroxide in alkaline solution to give catechol and flavone-3-carboxylic acid (see Baker, Jukes, and Subrahmanyam, *J.*, 1934, 1682), but it was found to be unchanged under the usual reaction conditions.

Experimental.

(Light petroleum refers to the fraction, b. p. 60—80°. M. p.s are uncorr. Microanalyses are by Mr. W. M. Eno, Bristol, and Drs. Weiler and Strauss, Oxford.)

o-(3 : 4 : 5-*Trimethoxybenzoyloxy*)*acetophenone*.—3 : 4 : 5-Trimethoxybenzoyl chloride (25 g.), *o*-hydroxyacetophenone (12·5 g.), and anhydrous pyridine (60 c.c.) were heated on the steam-bath for ½ hour, poured into dilute hydrochloric acid and ice, and the solid was collected, washed, and crystallised from ethanol, giving o-(3 : 4 : 5-*trimethoxybenzoyloxy*)*acetophenone* (23·1 g.) as long needles, m. p. 108° (Found, in material twice recrystallised from ethanol: C, 65·5; H, 5·5. $C_{18}H_{18}O_6$ requires C, 65·5; H, 5·5%).

o-*p*′-*Anisoyloxyacetophenone*.—This *ketone* was prepared from *p*-anisoyl chloride and *o*-hydroxyacetophenone as in the preceding case. It was obtained as plates (90%), m. p., after 4 crystallisations from ethanol, 113—114° (Found: C, 70·6; H, 5·1; OMe, 11·5. $C_{16}H_{14}O_4$·OMe requires C, 71·1; H, 5·2; OMe, 11·5%).

o-*Veratroyloxyacetophenone*.—This *compound* was similarly obtained as plates from ethanol (yield 84%) which, after several crystallisations from ethanol and then from benzene–light petroleum, had m. p. 129° [Found: C, 68·2; H, 5·3; OMe, 20·4. $C_{18}H_{18}O_5(OMe)_2$ requires C, 68·0; H, 5·3; OMe, 20·7%].

Benzoyl-o-hydroxybenzoylmethanes (IV; R = aryl).—These compounds were prepared as in the following example. o-(3 : 4 : 5-Trimethoxybenzoyloxy)acetophenone (22 g.) in anhydrous pyridine (80 c.c.) was treated at 40° with powdered potassium hydroxide (4 g.), and the mixture shaken vigorously for ½ hour. The thick yellow suspension of the potassium salt of the diketone was poured into excess of 20% acetic acid, and the yellow solid collected, washed, and dried. After crystallisation from ethanol–benzene, *o-hydroxybenzoyl-3′ : 4′ : 5′-trimethoxybenzoylmethane* (16 g.) was obtained as yellow needles, m. p. 135—136° (Found: C, 65·5; H, 5·5. $C_{19}H_{18}O_6$ requires C, 65·5; H, 5·5%). Benzoyl-o-hydroxybenzoylmethane, m. p. 120°, was obtained in 80% yield after one crystallisation from ethanol (Doyle *et al.*, *loc. cit.*, record an 83% yield of crude product). o-Anisoyl-o-hydroxybenzoylmethane was obtained in 62% yield, with m. p. 80°, after crystallisation from ethanol–benzene (cf. Baker and Besly, *J.*, 1940, 1106, who effected the migration with potassium carbonate in toluene). *p-Anisoyl-o-hydroxybenzoylmethane* formed yellow needles (68% yield), m. p. 111°, from ethanol (Found, in material twice crystallised from ethanol: C, 70·8; H, 5·2. $C_{18}H_{16}O_5$ requires C, 71·1; H, 5·2%). *o-Hydroxybenzoylveratroylmethane* formed yellow plates (72%), m. p. 130°, from benzene [Found, in material crystallised 4 times from benzene: C, 68·0; H, 5·2; OMe, 19·8. $C_{18}H_{16}O_5(OMe)_2$ requires C, 68·0; H, 5·3; OMe, 20·7%].

Arylidene Derivatives of Benzoyl-o-hydroxybenzoylmethanes (as VII and IX; R and R′ = aryl).—The arylidene derivatives of the benzoyl-o-hydroxybenzoylmethanes were prepared as in the following example. *o*-Hydroxybenzoyl-3′ : 4′ : 5′-trimethoxybenzoylmethane (11·6 g.) in ethanol (150 c.c.) was boiled for ½ hour with benzaldehyde (4·0 g.) and a few drops of piperidine. The pale yellow needles which separated after cooling to 0° were collected, washed, dried (12·7 g.), and recrystallised from benzene–light petroleum, giving *ω-o-hydroxybenzoyl-ω-3 : 4 : 5-trimethoxybenzoylstyrene* as colourless needles, m. p. 155° (Found: C, 71·9; H, 5·3. $C_{25}H_{24}O_6$ requires C, 71·7; H, 5·3%). Condensation of benzaldehyde with benzoyl-o-hydroxybenzoylmethane yielded *ω-benzoyl-ω-o-hydroxybenzoylstyrene*

(95%), as colourless prisms, m. p. 158—160°, from ethanol (Found: C, 80·0; H, 4·9. $C_{32}H_{16}O_5$ requires C, 80·5; H, 4·9%). Benzaldehyde and *o*-anisoyl-*o*-hydroxybenzoylmethane gave *ω-o-anisoyl-ω-o-hydroxybenzoylstyrene* as pale yellow needles, m. p. 125—126°, from ethanol (72% yield) (Found, in material crystallised several times from ethanol and then from benzene–light petroleum: C, 76·8; H, 5·2; OMe, 8·5. $C_{32}H_{16}O_5$·OMe requires C, 77·1; H, 5·0; OMe, 8·7%). Reaction of benzoyl-*o*-hydroxybenzoylmethane with *o*-anisaldehyde gave *ω-benzoyl-ω-o-hydroxybenzoyl-2-methoxystyrene* (84%) as colourless, rectangular prisms, m. p. 135—136°, from ethanol (Found, in substance crystallised twice from ethanol and once from benzene–light petroleum: C, 76·9; H, 5·1; OMe, 8·7. $C_{32}H_{16}O_5$·OMe requires C, 77·1; H, 5·0; OMe, 8·7%). From *p*-anisoyl-*o*-hydroxybenzoylmethane and benzaldehyde was obtained *ω-p-anisoyl-ω-o-hydroxybenzoylstyrene* (93%), which separated from ethanol as colourless prisms, m. p. 171—172° (Found: C, 76·9; H, 5·0; OMe, 8·7. $C_{32}H_{16}O_5$·OMe requires C, 77·1; H, 5·0; OMe, 8·7%). Benzoyl-*o*-hydroxybenzoylmethane and *p*-anisaldehyde gave *ω-benzoyl-ω-o-hydroxybenzoyl-4-methoxystyrene* (87%), which formed colourless needles, m. p. 133—134°, from ethanol (Found: C, 76·2; H, 5·0; OMe, 8·8. $C_{32}H_{16}O_5$·OMe requires C, 77·1; H, 5·0; OMe, 8·7%). Benzaldehyde and o-hydroxybenzoylveratroylmethane gave *ω-o-hydroxybenzoyl-ω-veratroylstyrene* (86%) which, after 5 crystallisations from ethanol (charcoal at first), was obtained as colourless prisms, m. p. 158—159° (Found: C, 74·0; H, 5·3; OMe, 15·7. $C_{32}H_{16}O_5(OMe)_2$ requires C, 74·2; H, 5·2; OMe, 16·0%). Veratraldehyde and benzoyl-*o*-hydroxybenzoylmethane gave *ω-benzoyl-ω-o-hydroxybenzoyl-3:4-dimethoxystyrene* (83%), which separated from benzene–light petroleum as colourless needles, m. p. 153—154° (Found, in material recrystallised from ethanol and again from benzene–light petroleum: C, 74·3; H, 5·4; OMe, 15·2. $C_{32}H_{16}O_5(OMe)_2$ requires C, 74·2; H, 5·2; OMe, 16·0%). 3:4:5-Trimethoxybenzaldehyde and benzoyl-*o*-hydroxybenzoylmethane gave *ω-benzoyl-ω-o-hydroxybenzoyl-3:4:5-trimethoxystyrene* (94%), which was crystallised twice from ethanol and obtained as fine, colourless needles, m. p. 150·5° (Found: C, 71·9; H, 5·1; OMe, 21·8. $C_{32}H_{16}O_5(OMe)_3$ requires C, 71·7; H, 5·3; OMe, 22·2%). *p*-Anisaldehyde and *o*-hydroxybenzoylveratroylmethane gave *ω-o-hydroxybenzoyl-4-methoxy-ω-veratroylstyrene* (83%); after several crystallisations from ethanol, this formed colourless needles which became yellow on melting at 131—132° (Found: C, 71·5; H, 5·2; OMe, 20·9. $C_{32}H_{16}O_5(OMe)_3$ requires C, 71·7; H, 5·3; OMe, 22·2%).

Preparation of 3-*Aroylflavones* (I and X; R and R′ = aryl).—These compounds were prepared from the corresponding benzoyl-*o*-hydroxybenzoylstyrenes by oxidation with selenium dioxide in amyl-alcoholic solution. The 3-aroylflavones were not always easily isolated from the reaction mixtures, and the procedure adopted for working up the product depended on whether the 3-aroyl group in the flavone was methoxylated (method *A*) or unsubstituted (method *B*).

Method A. 3-(3:4:5-*Trimethoxybenzoyl)flavone.* *ω-o*-Hydroxybenzoyl-*ω*-3:4:5-trimethoxybenzoylstyrene (6·2 g.) in *n*-amyl alcohol (100 c.c.) was refluxed with selenium dioxide (6·0 g.) for 17 hours, and the solution was then filtered hot, and the solid elementary selenium washed with a little hot amyl alcohol. To the filtrate was now added light petroleum and, after cooling to 0°, the solid product was collected and crystallised from ethanol (yield, 3·6 g.), and then from benzene–light petroleum, giving 3-(3:4:5-*trimethoxybenzoyl)flavone* as colourless prisms, m. p. 163° (Found: C, 72·1; H, 4·9; OMe, 22·4. $C_{32}H_{11}O_3(OMe)_3$ requires C, 72·1; H, 4·8; OMe, 22·4%).

Method B. 3-*Benzoyl-2′-methoxyflavone.* *ω*-Benzoyl-*ω-o*-hydroxybenzoyl-2-methoxystyrene (10 g.) in *n*-amyl alcohol (50 c.c.) was boiled under reflux for 12 hours with selenium dioxide (10 g.), and the filtered solution was subjected to steam-distillation to remove the amyl alcohol. The non-volatile residue was extracted into benzene, and the benzene solution was washed with aqueous sodium carbonate and water, dried, and distilled to dryness under diminished pressure, and the residual material was crystallised from ethanol (yield 6·1 g.). Further crystallisation from ethanol, then from benzene–light petroleum, and finally from ethanol gave the pure 3-*benzoyl-2′-methoxyflavone* as colourless plates, m. p. 139° (Found: C, 77·5; H, 4·6; OMe, 9·0. $C_{32}H_{16}O_3$·OMe requires C, 77·5; H, 4·5; OMe, 8·7%).

3-Benzoylflavone was prepared (method *B*) from *ω*-benzoyl-*ω-o*-hydroxybenzoylstyrene and crystallised from ethanol (yield 56%). Further crystallisation gave the pure compound as long, colourless needles, m. p. 130—131° (Found: C, 80·9; H, 4·3. Calc. for $C_{32}H_{16}O_3$: C, 80·8; H, 4·3%).

3-*o-Anisoylflavone*, prepared (method *A*) from *ω-o*-anisoyl-*ω*-benzoylstyrene, was crystallised from ethanol (yield 87%). For analysis it was crystallised several times from ethanol and then from benzene–light petroleum, giving colourless irregular prisms, m. p. 129° (Found: C, 78·1; H, 4·6; OMe, 8·7. $C_{32}H_{16}O_3$·OMe requires C, 77·5; H, 4·5; OMe, 8·7%).

3-*p-Anisoylflavone* was prepared (method *A*) from *ω-p*-anisoyl-*ω-o*-hydroxybenzoylstyrene and crystallised from ethanol (yield 70%). Recrystallisation from the same solvent gave the pure substance as colourless, irregular plates, m. p. 168° (Found: C, 77·3; H, 4·7; OMe, 8·7%).

3-*Benzoyl-4′-methoxyflavone* was prepared by the oxidation of *ω*-benzoyl-*ω-o*-hydroxybenzoyl-4-methoxystyrene (method *B*) and crystallised from ethanol (yield 72%). Further crystallisation from the same solvent gave colourless prisms, m. p. 143° (Found: C, 77·7; H, 4·8. $C_{32}H_{16}O_4$ requires C, 77·5; H, 4·5%).

3-*Veratroylflavone* was prepared by oxidation of *ω-o*-hydroxybenzoyl-*ω*-veratroylstyrene (method *A*), and after one crystallisation from ethanol gave a crude product (85%), m. p. 115—135°. A persistent impurity was removed by boiling the product in ethanol with charcoal and recrystallising it several times from the same solvent, giving, finally, small, colourless prisms which softened at 120° and melted at 165—166° (Found: C, 75·1; H, 4·7; OMe, 14·5. $C_{32}H_{16}O_3(OMe)_2$ requires C, 74·6; H, 4·7; OMe, 16·1%).

3-*Benzoyl-3′:4′-dimethoxyflavone* was prepared from *ω*-benzoyl-*ω-o*-hydroxybenzoyl-3:4-dimethoxystyrene (method *B*) and crystallised from ethanol (yield 71%). The pure substance was obtained by

crystallising twice from benzene–light petroleum, and then from ethanol, giving colourless prisms, m. p. 165° (Found : C, 74·4; H, 4·6; OMe, 15·6%).

3-*Benzoyl*-3′ : 4′ : 5′-*trimethoxyflavone*, prepared from ω-benzoyl-ω-*o*-hydroxybenzoyl-3 : 4 : 5-trimethoxystyrene by method *B*, was crystallised from ethanol (yield 57%). Further crystallisation from ethanol, then from benzene–light petroleum, and finally from ethanol, gave colourless prisms, m. p. 165° (Found : C, 72·7; H, 5·4; OMe, 20·9. $C_{22}H_{11}O_2(OMe)_3$ requires C, 72·1; H, 4·8; OMe, 22·4%).

4′-*Methoxy*-3-*veratroylflavone* was obtained by the oxidation of ω-*o*-hydroxybenzoyl-4-methoxy-ω-veratroylstyrene (method *A*) and crystallised from ethanol (89% yield). As in the case of 3-veratroylflavone this product contained a persistent impurity which was removed by boiling the ethanolic solution with charcoal and repeated crystallisation from the same solvent, giving finally colourless crystalline aggregates, m. p. 161° (Found : C, 72·2; H, 4·8%).

Reaction of Benzylamine with 3-*Benzoylflavone.*—3-Benzoylflavone (0·2 g.) in benzene (2 c.c.) was treated with benzylamine (0·14 g.), and the resulting yellow solution was heated on the water-bath for 8 hours. After removal of the benzene under diminished pressure the oily residue was treated with water and a little ethanol, and after solidification had occurred the product was crystallised twice from ethanol, giving yellow needles (0·09 g.), m. p. 98° (Found : C, 80·2; H, 5·6; N, 4·4. $C_{31}H_{17}O_2N$ requires C, 80·2; H, 5·8; N, 4·2%). This 2-*β-benzylaminocinnamoylphenol* (XI; R = Ph) exhibits a brilliant yellow fluorescence in ultra-violet light. The above ethanolic mother-liquors yielded by careful crystallisation a further amount (0·05 g.) of the same substance, and a smaller quantity of the more soluble and difficultly isolable benzobenzylamide (XII; R′ = Ph), which, after crystallisation from light petroleum, formed colourless needles, m. p. 106—107°, undepressed when mixed with a specimen, m. p. 106—107°, prepared by the method of Dermer and King (*J. Org. Chem.*, 1943, **8**, 169) from methyl benzoate and benzylamine.

Reaction of Benzylamine with 3-*o-Anisoylflavone.*—The flavone (1·0 g.) in anhydrous pyridine (10 c.c.) and benzylamine (0·65 g.) was boiled under reflux for 12 hours, cooled, poured into dilute hydrochloric acid, the yellow oil extracted into ether–benzene, the extracts were dried ($MgSO_4$) and the solvents removed finally under diminished pressure. The yellow product was crystallised twice from ethanol (yield after one crystallisation, 0·73 g.), giving yellow needles, m. p. 98°, undepressed on admixture with the specimen of 2-*β*-benzylaminocinnamoylphenol prepared as above. The material (0·62 g.) contained in the alcoholic mother-liquors was crystallised from ethanol and then 3 times from benzene–light petroleum, giving *o-anisobenzylamide* as colourless prisms, m. p. 87—88° (Found : C, 74·9; H, 6·5; N, 5·1; OMe, 12·7. $C_{14}H_{13}ON{\cdot}OMe$ requires C, 74·7; H, 6·2; N, 5·8; OMe, 12·9%).

Reaction of Benzylamine with 3-*Benzoyl-2′-methoxyflavone.*—The flavone (1·0 g.) was treated with benzylamine as in the previous case. The product was crystallised once from ethanol (15 c.c.), giving 2-(*β-benzylamino-2-methoxycinnamoyl*)*phenol* as greenish-yellow cubes (0·88 g.), which, after further crystallisation from ethanol and then from benzene–light petroleum, had m. p. 125° (Found : C, 76·9; H, 5·9; N, 3·9; OMe, 8·6. $C_{32}H_{14}O_4{\cdot}OMe$ requires C, 76·9; H, 5·9; N, 3·9; OMe, 8·6%). Dilution of the mother-liquors with water gave crude benzobenzylamide (0·57 g.), which, after two recrystallisations from ethanol, had m. p. and mixed m. p. 105—106°.

Reaction of Benzylamine with 3-p-*Anisoylflavone.*—Treatment of this flavone (1 g.) in pyridine (25 c.c.) with benzylamine (0·65 g.) as in the previous cases gave a mixture from which was isolated, by crystallisation from ethanol, 2-*β*-benzylaminocinnamoylphenol (total yield 0·77 g.) as yellow needles, m. p. and mixed m. p. 98°. The mother-liquors were diluted, and after being boiled with charcoal, deposited fine, colourless needles of *p*-anisobenzylamide (0·1 g.), m. p. 125—128°, raised to 131° after 2 further crystallisations (Beckmann, *Ber.*, 1904, **37**, 4138, records m. p. 131°).

Reaction of Benzylamine with 3-*Benzoyl-4′-methoxyflavone.*—The flavone (1·0 g.) in benzene (10 c.c.) was treated with benzylamine (0·65 g.) as in the previous cases, the reaction product was shaken with cold ethanol (15 c.c.), and the solid 2-(*β-benzylamino-4-methoxycinnamoyl*)*phenol* (0·45 g.) collected. Two recrystallisations from ethanol gave the pure compound as yellow needles, m. p. 127—127·5° (Found : C, 76·5; H, 6·1; N, 4·0. $C_{33}H_{21}O_3N$ requires C, 76·9; H, 5·9; N, 3·9%). The ethanolic mother-liquors gave by concentration a further quantity (0·32 g.) of this substance, and the final liquors, after dilution with water, treatment with charcoal, and filtration while hot, yielded a small quantity (*ca.* 0·1 g.) of benzobenzylamide, m. p. and mixed m. p. 107°.

Reaction of Benzylamine with 3-*Veratroylflavone.*—The flavone (1·0 g.) in pyridine (10 c.c.) was boiled under reflux with benzylamine (0·6 g.) for 16 hours. The reaction product isolated in the usual way was dissolved in boiling ethanol, and on cooling deposited yellow needles of 2-(*β*-benzylaminocinnamoyl)-phenol (0·74 g.), m. p. and mixed m. p. 98°. The mother-liquors were concentrated, and when kept deposited crude *veratrobenzylamide* (0·5 g.), which after twice crystallising from aqueous methanol formed colourless needles, m. p. 137° (Found : C, 71·2; H, 6·3; N, 4·9; OMe, 23·6. $C_{16}H_{17}ON(OMe)_2$ requires C, 70·8; H, 6·3; N, 5·2; OMe, 22·9%).

Reaction of Benzylamine with 3-*Benzoyl*-3′ : 4′-*dimethoxyflavone.*—The flavone (1·0 g.) in pyridine (10 c.c.) was boiled with benzylamine for 15 hours. The product, isolated as in the previous cases, was crystallised from ethanol, giving yellow plates (0·92 g.) of 2-(*β-benzylamino*-3 : 4-*dimethoxycinnamoyl*)-*phenol*, which, after further crystallisation from benzene–light petroleum and again from ethanol, had m. p. 144° (Found : C, 74·1; H, 6·0; N, 3·6; OMe, 15·6. $C_{33}H_{21}O_3N(OMe)_2$ requires C, 74·0; H, 5·9; N, 3·6; OMe, 15·9%). The mother-liquors yielded benzobenzylamide (0·37 g.), which, after two recrystallisations from aqueous ethanol, had m. p. and mixed m. p. 105—106°.

Reaction of Benzylamine with 3-(3 : 4 : 5-*Trimethoxybenzoyl*)*flavone.*—The flavone (1·0 g.), pyridine (10 c.c.), and benzylamine (0·55 g.) were boiled together for 9 hours, and the products isolated in the usual way and crystallised from ethanol (10 c.c.). 2-(*β*-Benzylaminocinnamoyl)phenol (0·63 g.) separated as

yellow needles, which after recrystallisation from ethanol had m. p. and mixed m. p. 98°. The diluted mother-liquors were extracted with ether, and the extract deposited colourless needles of **3 : 4 : 5-*trimethoxybenzobenzylamide*** (0·15 g.), which, after crystallising 3 times from aqueous ethanol, formed colourless needles, m. p. 141° [Found: C, 67·7; H, 6·3; N, 4·8; OMe, 31·3. $C_{18}H_{19}ON(OMe)_3$ requires C, 67·3; H, 6·9; N, 4·6; OMe, 30·7%]. Further quantities of the phenol (0·13 g.) and of the amide (0·28 g.) were obtained by suitable crystallisation of the mother-liquors.

Reaction of Benzylamine with 3-Benzoyl-3′ : 4′ : 5′-trimethoxyflavone.—The flavone (1·0 g.) was treated with benzylamine as in the previous case, and the isolated reaction product was crystallised from ethanol, giving **2-(*β-benzylamino*-3′ : 4′ : 5′-*trimethoxycinnamoyl*)*phenol*** (0·80 g.), which, after twice crystallising from ethanol, formed bright yellow prisms, m. p. 115° [Found: C, 71·7; H, 5·9; N, 3·4; OMe, 21·6. $C_{26}H_{19}O_3N(OMe)_3$ requires C, 71·6; H, 6·0; N, 3·3; OMe, 22·2%]. Dilution of the mother-liquors gave crude benzobenzylamide (0·5 g.), which after crystallisation from aqueous ethanol had m. p. and mixed m. p. 106—107°.

Reaction of Benzylamine with 4′-Methoxy-3-veratroylflavone.—The flavone (1·0 g.), pyridine (10 c.c.), and benzylamine (0·55 g.) were boiled for 16 hours, and the product, isolated as usual, was crystallised from ethanol, giving **2-(*β*-benzylamino-4-methoxycinnamoyl)phenol** (0·75 g.), m. p. and mixed m. p. 126—127°. Addition of water to the mother-liquor gave veratrobenzylamide, which after crystallisation from aqueous methanol was obtained as needles, m. p. and mixed m. p. 137°.

3-*o*-*Hydroxybenzoylflavone.*—3-*o*-Anisoylflavone (1·0 g.) was boiled under reflux with glacial acetic acid (30 c.c.) and aqueous hydrobromic acid (40 c.c.; 48%) for 8 hours. The solid which separated after the addition of water (200 c.c.) was collected, washed, dried (0·91 g.), and crystallised 3 times from ethanol, giving colourless plates, m. p. 199—200° (Found, in material dried at 100° for ½ hour: C, 77·6; H, 4·5. $C_{22}H_{14}O_4$ requires C, 77·1; H, 4·1%). This **3-*o*-*hydroxybenzoylflavone*** gives no colour with ferric chloride in alcohol, and shows only very weakly phenolic properties. It is insoluble in aqueous sodium hydroxide, but forms a sodium salt in aqueous-acetone solution of this alkali.

The authors are grateful to the Department of Scientific and Industrial Research for a maintenance allowance (awarded to F. G.), and to the Directors of Imperial Chemical Industries Limited for a grant.

THE UNIVERSITY, BRISTOL. [*Received, June 19th, 1950.*]

---

531. *The Crystal Structure of Thorium Tetrabromide.*

By R. W. M. D'EYE.

The crystal structure of thorium tetrabromide has been determined by means of *X*-ray powder diffraction photographs. The structure is body-centred tetragonal, space group $D_{4h}^{19} - I4_1/amd$, with a, c, c/a, and ρ (calc.) equal to 8·945 A., 7·930 ± 0·005 A., 0·887, and 5·69 g./c.c., respectively. There are 4 molecules per unit cell.

Positions have been found for the atoms such that the calculated are in good agreement with the observed intensities. The Th–Br (nearest neighbour) distance is 2·57 A. and Th–Br (second nearest neighbour) is 3·31 A. It would appear that the bromide, like the chloride, is partially covalent in character. The arrangement of the four nearest bromine atoms around the thorium atom is shown to be a distorted square or an extremely flattened tetrahedron with Br–Th–Br angles 93·8° and 150·2°.

THE crystal structure of thorium tetrachloride has been found by Mooney (*Acta Cryst.*, 1949, **2**, 189) to be a body-centred tetragonal lattice with cell dimensions $a = 8·473$, $c = 7·468$ A. The number of molecules per unit cell is 4, and the space group is $D_{4h}^{19} - I4_1/amd$. It was found that this chloride was isomorphous with uranium tetrachloride. The structure of thorium tetrabromide has not been worked out hitherto, but it is now found that this compound is isostructural with the tetrachloride.

EXPERIMENTAL.

Thorium tetrabromide was prepared by direct union of the elements *in vacuo*. A sample was transferred, *in vacuo*, to thin-walled Pyrex *X*-ray capillary tubes of approx. 0·3 mm. diameter. Powder diffraction photographs were taken in the usual manner by use of standard *X*-ray equipment, a 9-cm. Unicam camera, and filtered Cu-$K\alpha$ radiation. The resulting photographs were measured by using a steel scale and vernier, and the intensities were visually estimated.

From the Bragg relationship $\lambda = 2d \sin \theta$, the interplanar spacings d were calculated. By use of a Bunn chart, the diffraction pattern was successfully indexed on the basis of tetragonal cell of axial ratio, c/a, approx. 0·9. The cell constants a and c were then calculated to be 8·945 and 7·930 A. ± 0·005 A., respectively ($c/a = 0·887$). The density, calculated on the assumption that there are 4 mols. per unit cell, is 5·69 g./c.c., which is in close agreement with the experimentally determined value of 5·67 g./c.c. (Moissan and Martinsen, *Compt. rend.*, 1905, **140**, 1513).

From consideration of the indices of the planes the following regularites were observed:

(*hkl*) present if $h + k + l = 2n$
(*hk*0) ,, $h = 2n$ and $k = 2n$
(0*kl*) present if $k + l = 2n$
(*hkl*) ,, $l = 2n$ and $2h + l = 4n$

This indicates a body-centred tetragonal cell of space group $D_{4h}^{19} - I4_1/amd$. For this space group the positions of the atoms, as given in Internationale Tabellen, Vol. I, are :

4-fold sets (*a*) and (*b*)	parameters 000 or 00$\frac{1}{2}$					16-fold sets (*f*) and (*g*)	parameters $x\frac{1}{4}\frac{1}{8}$ or xxo		
8- ,, (*c*) ,, (*d*)	,, $0\frac{1}{4}\frac{1}{8}$ or $0\frac{1}{4}\frac{3}{8}$					16- ,, (*h*)	,, oyz		
8- ,, (*e*)	,, $00z$								

The four thorium atoms are necessarily in one of the four-fold sets (*a*) and (*b*). If set (*a*) is chosen, these atoms will have the positions 000, $0\frac{1}{2}\frac{1}{4}$, $\frac{1}{2}\frac{1}{2}\frac{1}{4}$, and $\frac{1}{2}0\frac{3}{4}$.

Thorium with parameters 000 makes no contribution to planes with $2h + l = 4n + 2$, whereas for planes with $2h + l = 4n$, $2h + l = 4n + 1$ the contributions are respectively $A = 4f_{Th}$ and $B = 0$, $A = 2f_{Th}$ and $B = -A$, and $A = B = 2f_{Th}$, where f_{Th} is the scattering factor for thorium.

Plane (202) is of medium intensity, whereas planes (402), (422), and (314) are definitely not observed. The thorium contribution to these planes is zero ; thus it is possible to eliminate any set of positions for bromine atoms which does not give a moderate structure amplitude for (202) and a very small amplitude for (402). This at once eliminates the 16-fold set (*g*) with parameters *xxo*.

If the bromine atoms were distributed as in the 8-fold set (*e*) with parameters *ooz*, the bromine contribution must necessarily reinforce the thorium contribution for planes (*hk*0). All observed (*hk*0) planes were either very weak or absent, indicating that the bromine contribution must be near maximum and out of phase with the thorium contribution. This therefore eliminates the possibility of two 8-fold sets (*e*) or a combination of an 8-fold set (*e*) with either an 8-fold set (*c*) or (*d*). More detailed consideration of the 8-fold sets (*c*) and (*d*) rules out the possibility of bromine being in either of these two sets. Also it is found that the *z* parameter cannot be $\frac{1}{4}$ or $\frac{1}{8}$, which eliminates the 16-fold set (*f*) as well.

We are left therefore with the 16-fold set (*h*) with parameters *oyz*. Rough values for *y* and *z* were obtained by comparing observed and calculated structure amplitudes for planes (*hk*0). These values were refined by further comparison of calculated and observed amplitudes for all the sensitive planes. The final values arrived at were : $y = 100°$ and $z = 330°$. The bromine atoms are accordingly in positions :

$$0yz\,;\ 0\bar{y}z\,;\ y0\bar{z}\,;\ \bar{y}0\bar{z}\,;\ 0,\ \tfrac{1}{2}+y,\ \tfrac{1}{2}-z\,;\ 0,\ \tfrac{1}{2}-y,\ \tfrac{1}{2}-z\,;\ y,\ \tfrac{1}{2},\ \tfrac{1}{2}+z\,;\ \bar{y},\ \tfrac{1}{2},\ \tfrac{1}{2}+z\ (\text{all} + \tfrac{1}{2}\tfrac{1}{2}\tfrac{1}{2}).$$

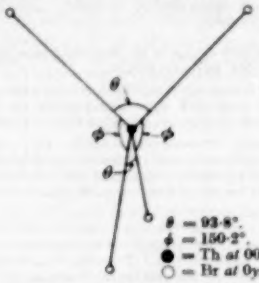
It is seen from the table that the calculated intensities I_c, where $I_c \propto F^2 m$, F being the structure factor and *m* the multiplicity constant, are in good agreement with the observed intensities. In comparing intensities of reflections at widely different scattering angles allowance should, however, be made for the effects of absorption and polarization. The calculated values of interplanar planar spacing d_c are seen to be in agreement with the observed values.

θ	*hkl*	$d_{obs.}$	$d_{calc.}$	$I_{obs.}$	$I_{calc.}$		θ	*hkl*	$d_{obs.}$	$d_{calc.}$	$I_{obs.}$	$I_{calc.}$	
7·71	101	5·78	5·93	W	13·8		32·6	611	1·4363	1·4458	VVW	6·4	
10·19	200	4·39	4·47	W	12·0			334		1·4443		0·0	
13·45	112	3·343	3·359	W−	15·3		33·32	523	1·4084	1·4064	M−S	14·4	41·0
15·23	202	2·959	2·967	M	29·3			424		1·4081		26·6	
16·28	301	2·772	2·791	M−	28·4		35·29	622	1·3381	1·3321	W+	1·5	38·3
17·93	103	2·523	2·535	M	30·6			325		1·3363		34·8	
19·26	321	2·354	2·367	M−	26·8		36·05	631	1·3134	1·3149	W−	20	22·4
19·8	312	2·292	2·302	M	42·5			514		1·3137		2·4	
20·47	213	2·2198	2·2064	W	39·8		36·46	116	1·3004	1·2938	VW+	18	
20·47	400	2·2198	2·2361	W	42·3		37·03	415	1·2831	1·2804	M	30·4	46·8
21·71	411	2·0979	2·0925	VVW	16·4			613		1·2850		16·4	
23·01	420	1·9844	2·000	VVW	12·1		38·78	543	1·2332	1·2350	M−	43·6	46·4
	004		1·9826	Abs	0·4	3·8		444		1·2360		2·8	
	303		1·9780		3·4		39·57	721	1·2123	1·2140	VW+	28·0	30·0
24·66	332	1·8586	1·8614	M−	27·1			534		1·2133		2·0	
25·29	323	1·8147	1·8089	VVW	0·01	14·21	40·33	604	1·1931	1·1915	VW	7·2	10·4
	204		1·8126		14·2			435		1·1868		3·2	
	503		1·4815		29·9		43·44	336	1·1221	1·1198	M−	1·2	17·8
31·51	433	1·4812	1·4815	S−	17·4	49·4		107		1·1240		16·6	
	404		1·4834		2·1								

Discussion.

From the above evidence it would appear that thorium tetrabromide, like the chloride (Mooney, *loc. cit.*), has a body-centred tetragonal type structure with unit cell dimensions as given above. The thorium atom is surrounded by eight bromine atoms, four at distances of 2·57 A. and four at 3·31 A. The smallest Br–Br distance is 3·34 A. Covalency being assumed for thorium tetrabromide and tetrachloride, the atomic radius of thorium can be calculated as 0·9 A. and 0·86 A., respectively. Pauling's values being assumed for the ionic radius of chlorine and bromine, and a pure ionic nature assumed for both halides, the radius of thorium can be calculated as 0·62 A. and 0·65 A. for the chloride and bromide, respectively. In the completely ionic structure, ThO_2, the ionic radius for Th^{4+} is 1·02 A. On the basis, therefore, of the bromine atoms' not being in a close-packed arrangement around the thorium atom, indicated by the unequal

Th–Br distances, and the significantly smaller radius of thorium in the chloride and bromide than in the dioxide, it is reasonable to assume that the bromide, like the chloride, is, at least, partially covalent in character.



The four nearest bromine atoms (Br–Br = 3·76 A.) form a configuration around the thorium atom which can be described as a rhombic bisphenoid (see figure). The halogen–Th–halogen angles calculated from the observed data are 93·8° and 150·2° for the tetrabromide and 93·4° and 149° for the tetrachloride.

The author thanks Dr. J. S. Anderson for helpful advice and Mr. R. C. Blakey for help in taking the *X*-ray powder photographs, also the Director of the Atomic Energy Research Establishment, Harwell, for permission to publish the paper.

A.E.R.E., Harwell. [*Received, May 12th*, 1950.]

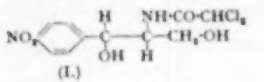
---

532. *Nuclear Halogen-containing Analogues of Chloramphenicol.*

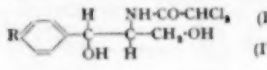
By Ng. Ph. Buu-Hoï, Ng. Hoán, Pierre Jacquignon, and Ng. H. Khoï.

In continuation of earlier work on analogues of chloramphenicol, molecules derived from chloramphenicol by replacement of the nitro-group by fluorine and iodine have been synthesised for biological testing. In connection with this problem, 1-*p*-chloro- and 1-*p*-bromo-phenyl-2-dichloroacetamidoethanol were also prepared.

Notwithstanding the now widespread clinical use of chloramphenicol (chloromycetin), little definite is yet known about the nature of its antibiotic activity. However, its chemical constitution as an optically active form of *threo*-2-dichloroacetamido-1-*p*-nitrophenylpropane-1 : 3-diol (I) (Controulis, Rebstock, and Crooks, *J. Amer. Chem. Soc.*, **1949**, **71**, 2463) strongly suggests that the versatile antibacterial and virucidal effects of that drug might be caused by biochemical



(I.)

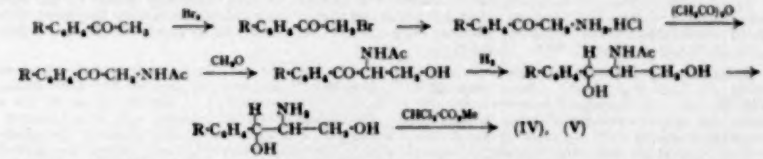


(II; R = Br.) (III; R = Cl.) (IV; R = Cl.) (V; R = I.)

competition with several important metabolites of the aromatic series which bear a more or less similar structure. A tentative, but by no means exhaustive, list of such metabolites would include *p*-aminobenzoic acid, β-phenylalanine, tyrosine, and even tryptophan, the last particularly with regard to antiviral activity. *p*-Nitrobenzoic acid and its esters are already known to antagonise *p*-aminobenzoic acid (Miller, *J. Pharmacol. Exp. Therap.*, 1941, **71**, 14); and substances such as β-hydroxyphenylalanine, *m*-fluorophenylalanine, and 3-fluorotyrosine are known to be competitive antagonists for β-phenylalanine (Beerstecher and Shive, *J. Biol. Chem.*, **1946**, **164**, 53; Mitchell and Niemann, *J. Amer. Chem. Soc.*, **1947**, **60**, 1232). These considerations led us to think that the antibiotic properties of chloramphenicol might not be specific, and that other substances with similar constitution might also be active. This assumption has now proved to be correct, as (±)-*threo*-2-dichloroacetamido-1-*p*-bromophenylpropane-1 : 3-diol (II) was found only about five times less active than (±)-chloramphenicol against a variety of micro-organisms including *Staphylococcus aureus*, *Escherichia coli*, and *B. paratyphosus*

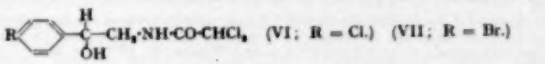
B. Owing to its relatively low toxicity in animals, this compound is now undergoing clinical trial. The activity of (±)-*threo*-2-dichloroacetamido-1-*p*-chlorophenylpropane-1 : 3-diol (III) was somewhat inferior, although of the same nature. The presence of a substituent in the *para*-position seems to be of paramount importance, since (±)-*threo*-2-dichloroacetamido-1-*m*-nitrophenylpropane-1 : 3-diol (Buu-Hoï and Khoï, *Compt. rend.*, 1949, **229**, 1343; 1950, **230**, 967) was inactive.

In view of these promising results, we have now prepared the *p*-fluoro- (IV) and *p*-iodo-analogues (V) for biological testing. The method used started from *p*-fluoro- and *p*-iodo-acetophenone, and followed the pattern of the Long–Troutman synthesis of chloramphenicol (*J. Amer. Chem. Soc.*, 1949, **71**, 2469) and of the synthesis of (II) and (III) (Buu-Hoï, Hoán, Jacquignon, and Khoï, *Compt. rend.*, 1950, **230**, 662):



Whereas formaldehyde and acetophenone give a di(hydroxymethyl) compound (Fuson and McKewer, *J. Amer. Chem. Soc.*, 1938, **60**, 2935), only one hydroxymethyl group could be introduced in the present instances. This behaviour seems to be general to α-acetamidoacetophenones, and is reminiscent of the inertia towards substitution found of the tertiary hydrogen atom of *iso*propyl groups (cf. Ziegler *et al.*, *Annalen*, 1942, **551**, 80). It is also noteworthy that the Ponndorf–Meerwein reductions of α-acetamino-*p*-fluoro-β-hydroxy- and α-acetamino-β-hydroxy-4-iodopropiophenone led to a single secondary alcohol in each case. These reaction products are assumed to belong to the *threo*- and not to the *erythro*-series, both because of analogy with the behaviour of α-acetamido-β-hydroxy-*p*-nitropropiophenone (Long and Troutman, *loc. cit.*), and because of the antibacterial activity of (IV) and (V). Unexpectedly, the latter compound had only about one-thirtieth of the activity of (±)-chloramphenicol towards *Staph. aureus* and *E. coli*.

A striking feature of the biochemistry of chloramphenicol is that whilst 2-dichloroacetamido-2-*p*-nitrophenylpropane-1 : 3-diol (a position-isomer very close to chloramphenicol) was completely inactive (Ruoff and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 1417), suppression of the



terminal hydroxymethyl group has no such drastic effect, as (±)-2-dichloroacetamido-1-*p*-nitrophenylethanol (Buu-Hoï and Khoï, *loc. cit.*) is now found to produce complete inhibition of the growth of *Staph. aureus* and *E. coli*. at a concentration of 6×10^{-4}. This led us to describe here two analogous compounds, (±)-1-*p*-chloro- (VI) and (±)-1-*p*-bromophenyl-2-dichloroacetamidoethanol (VII). These were prepared from *p*-chloro- and *p*-bromo-acetophenone by a method similar to that already outlined in a previous paper (Buu-Hoï and Khoï, *loc. cit.*, 1950).

Experimental.

(±)-2-*Acetamido*-1-p-*chlorophenylethanol*.—A solution of α-acetamido-*p*-chloroacetophenone (Buu-Hoï, Hoán, Jacquignon, and Khoï, *loc. cit.*) (20 g.) and freshly distilled aluminium *iso*propoxide (23 g.) in anhydrous *iso*propyl alcohol (200 c.c.) was gently refluxed, and the acetone formed removed through an efficient Vigreux column. After 24 hours, no more acetone could be detected in the distillate by means of sodium hydrogen sulphite; water (20 c.c.) was then added and the mixture boiled for some minutes. The solid obtained was filtered off and extracted 3 times with small quantities of boiling *iso*propyl alcohol. The liquid from the filtration was combined with the extracts and the whole was concentrated in a vacuum. The *compound* obtained after cooling formed fine colourless microscopic needles (15 g.), m. p. 122°, from *iso*propyl alcohol (Found: C, 56·0; H, 5·6. $C_{11}H_{12}O_3NCl$ requires C, 56·2; H, 5·6%).

(±)-2-*Amino*-1-p-*chlorophenylethanol*.—The foregoing amide (10 g.) was heated for 1 hour on a water-bath with concentrated hydrochloric acid (10 g.) and water (100 c.c.). The solution obtained was chilled, and basified with ice-cooled 20% aqueous sodium hydroxide. The solid *amine* precipitated (8 g.) was collected, washed with a little ice-water, and dried in a vacuum; it formed colourless needles, m. p. 94°, from benzene (Found: C, 55·8; H, 6·0. $C_8H_{10}ONCl$ requires C, 55·9; H, 5·8%).

(±)-1-p-*Chlorophenyl*-2-*dichloroacetamidoethanol* (VI).—A mixture of the foregoing amine (5 g.) with methyl dichloroacetate (6 g.) was heated at 90° for 3 hours, and the reaction product poured into ligroin; the solid obtained on scratching (5 g.) crystallised in shiny colourless needles, m. p. 85°, from ethyl acetate or ligroin (Found : C, 42·3; H, 3·6. $C_{10}H_{10}O_2NCl_3$ requires C, 42·4; H, 3·5%).

(±)-2-*Acetamido*-1-p-*bromophenylethanol*.—A solution of α-acetamido-*p*-bromoacetophenone (Buu-Hoï, Hoán, Jacquignon, and Khoï, *loc. cit.*) (25 g.) and aluminium *iso*propoxide (31 g.) in *iso*propyl alcohol (200 c.c.) was treated as in the case of the chlorine analogue. The *product* obtained (20 g.) formed fine colourless needles, m. p. 142°, from *iso*propyl alcohol (Found : C, 46·5; H, 4·7. $C_{10}H_{12}O_2NBr$ requires C, 46·5; H, 4·65%).

(±)-2-*Amino*-1-p-*bromophenylethanol*.—This *amine* (4 g.), obtained as usual from the foregoing compound (7 g.) by means of 10% hydrochloric acid, formed colourless needles, m. p. 112°, from benzene (Found : C, 44·4; H, 4·8. $C_8H_{10}ONBr$ requires C, 44·4; H, 4·6%).

(±)-1-p-*Bromophenyl*-2-*dichloroacetamidoethanol*.—A mixture of the foregoing amine (1 g.) and methyl dichloroacetate (5 g.) was heated for 3 hours at about 90°; the *amide* obtained after treatment with ligroin crystallised in fine colourless needles, m. p. *ca.* 85°, from benzene (Found : C, 36·4; H, 3·2. $C_{10}H_{10}O_2NCl_2Br$ requires C, 36·6; H, 3·1%).

α-*Acetamido*-p-*fluoroacetophenone* [with Miss D. Lavit].—A mixture of α-bromo-*p*-fluoroacetophenone (115 g.) (cf. Lutz *et al.*, *J. Org. Chem.*, 1947, **12**, 617; Buu-Hoï, Hoán, and Jacquignon, *Rec. Trav. chim.*, 1949, **68**, 781) and hexamethylenetetramine (80 g.) in dry chlorobenzene (1 l.) was stirred at 50° for 4 hours, and kept overnight at room temperature. The hexamethylenetetramine salt of α-bromo-*p*-fluoroacetophenone (170 g.) thus obtained was filtered off, and gave after crystallisation colourless needles, m. p. about 184—185° (decomp.), from ethanol. The crude quaternary salt (165 g.) was stirred with ethanol (350 c.c.) and concentrated hydrochloric acid (300 c.c.) at room temperature for 20 hours. Concentration *in vacuo* and subsequent chilling gave a colourless crystalline magma of 4-fluorophenacylamine hydrochloride (60 g.), which was filtered off and washed with cold ethanol. To a well-stirred solution of this crude salt (50 g.) in ice-water (200 c.c.), acetic anhydride (50 g.) and then a solution of sodium acetate (74 g.) in ice-water (150 c.c.) were cautiously added. Stirring was continued for a further hour at room temperature, and the solid obtained filtered off and recrystallised in ethyl acetate. α-*Acetamido*-p-*fluoroacetophenone* (15 g.) formed shiny colourless leaflets, m. p. 155° (Found : C, 58·6; H, 5·0. $C_{10}H_{10}O_2NF$ requires C, 61·5; H, 5·1%).

α-*Acetamido*-p-*fluoro*-β-*hydroxypropiophenone*.—A mixture of α-acetamido-*p*-fluoroacetophenone (10 g.), ethanol (40 c.c.), and 30% aqueous formaldehyde (10 c.c.) was stirred with sodium hydrogen carbonate (0·5 g.) for 2 hours at 35°. The clear solution thus obtained was poured into ice-water and extracted several times with ether. The *ketone* obtained after evaporation of the ether (10 g.) crystallised in fine colourless needles, m. p. 128°, from ethyl acetate (Found : C, 58·6; H, 5·5. $C_{11}H_{12}O_3NF$ requires C, 58·7; H, 5·3%).

(±)-threo-2-*Acetamido*-1-p-*fluorophenylpropane*-1 : 3-*diol*.—A solution of the foregoing compound (9 g.) and aluminium *iso*propoxide (13 g.) in anhydrous *iso*propyl alcohol (100 c.c.) was gently refluxed for 7 hours with removal of acetone. The *amide* (5 g.) obtained after the usual treatment formed colourless needles, m. p. 144°, from ethyl acetate (Found : C, 58·0; H, 6·2. $C_{11}H_{14}O_3NF$ requires C, 58·1; H, 6·1%). There was no sign of the presence of a stereoisomer formed during this reduction.

(±)-threo-2-*Amino*-1-p-*fluorophenylpropane*-1 : 3-*diol*.—Hydrolysis of the foregoing amide by hydrochloric acid in the usual way, and basification of the reaction product, gave the free *amine*, crystallising in fine colourless prisms, m. p. 121°, from benzene (Found : C, 58·1; H, 6·4. $C_9H_{12}O_2NF$ requires C, 58·3; H, 6·4%).

(±)-threo-2-*Dichloroacetamido*-1-p-*fluorophenylpropane*-1 : 3-*diol* (IV).—This *compound*, obtained from treatment of the foregoing carefully dried amine with methyl dichloroacetate in the usual way, formed fine colourless prisms, m. p. 131—132°, from benzene (Found : C, 44·6; H, 4·3. $C_{11}H_{12}O_3NCl_2F$ requires C, 44·5; H, 4·1%).

α-*Acetamido*-p-*iodoacetophenone*.—α-Bromo-*p*-iodoacetophenone (Kimura, *Ber.*, 1934, **67**, 395) was best prepared by bromating *p*-iodoacetophenone in chloroform in daylight; 80 g. of this compound, allowed to react with hexamethylenetetramine (40 g.) in chlorobenzene (175 c.c.) at 50° in the usual way, yielded 120 g. of the quaternary *salt*, *p*-I·C_6H_4·CO·$CH_2Br.N_4(CH_2)_6$, crystallising in fine colourless prisms, m. p. *ca.* 218—220° (decomp.), from ethanol, which become pink in the air (Found : N, 11·5. $C_{14}H_{17}N_4BrI$ requires N, 11·8%). *p*-Iodophenacylamine hydrochloride (98 g.) was obtained by treatment of the foregoing quaternary salt (115 g.) with hydrochloric acid (180 g.) in ethanol (200 c.c.) in the usual way. A solution of this hydrochloride (60 g.) in ice-water (150 c.c.) was acetylated by acetic anhydride (40 g.) and sodium acetate (60 g. in 100 c.c. of ice-water); after crystallisation from ethanol, the *acetyl* compound formed fine colourless needles (26 g.), m. p. 193—194° (Found : C, 39·5; H, 3·5. $C_{10}H_{10}O_2NI$ requires C, 39·6; H, 3·3%).

α-*Acetamido*-β-*hydroxy*-p-*iodopropiophenone*.—A mixture of the foregoing amide (23 g.) in ethanol (100 c.c.), 30% aqueous formaldehyde (25 c.c.), and pure sodium hydrogen carbonate (1 g.) was stirred for 2 hours at 35°; the reaction product was poured into water, and the precipitated *compound* (20 g.) recrystallised from ethyl acetate, giving colourless needles, m. p. 179° (decomp.), becoming pink in the air (Found : C, 39·5; H, 3·7. $C_{11}H_{12}O_3NI$ requires C, 39·6; H, 3·6%).

(±)-threo-2-*Acetamido*-1-p-*iodophenylpropane*-1 : 3-*diol*.—The foregoing compound (17 g.), reduced in the usual way with aluminium *iso*propoxide (2 g.) in *iso*propyl alcohol (200 c.c.), yielded the *diol* (10 g.), crystallising in colourless needles, m. p. 166°, from ethyl acetate (Found : C, 39·2; H, 4·3. $C_{11}H_{14}O_3NI$ requires C, 39·4; H, 4·2%).

(±)-threo-2-*Amino*-1-p-*iodophenylpropane*-1 : 3-*diol*.—Hydrolysis of the foregoing *acetyl* compound (4·5 g.) with hydrochloric acid in the usual way, gave on basification the free *amine* (2·5 g.), crystallising in colourless needles, m. p. 119—120°, from benzene (Found: C, 36·6; H, 4·3. $C_9H_{12}O_2NI$ requires C, 36·5; H, 4·1%).

(±)-threo-2-*Dichloroacetamido*-1-p-*iodophenylpropane*-1 : 3-*diol* (V).—This *compound* (1·5 g.), obtained from the foregoing amine (1·5 g.) and methyl dichloroacetate, formed fine colourless prisms, m. p. 103—104°, from benzene (Found: C, 32·6; H, 3·2. $C_{11}H_{11}O_4NCl_2I$ requires C, 32·7; H, 3·0%).

Thanks are offered to Messrs. La Société Belge de l'Azote (Liège) and to Dr. J. Guigan (Paris) for some microbiological assays, and to Miss Patricia F. Boshell, M.A. (Oxon.), for assistance in this work.

The Radium Institute, University of Paris. [*Received, June 30th*, 1950.]

---

533. *Deoxy-sugars. Part XIII. Some Observations on the Feulgen Nucleal Reaction.*

By W. G. Overend.

Some of the problems of the Feulgen nucleal reaction have been studied. The intensities of the colours produced when Schiff's reagent is added to some 2-deoxy-pentose and -hexose derivatives have been compared with those produced by adding the reagent to the normal sugar analogue. The value of the reaction in indicating the location in cells of deoxypentose nucleic acids is discussed.

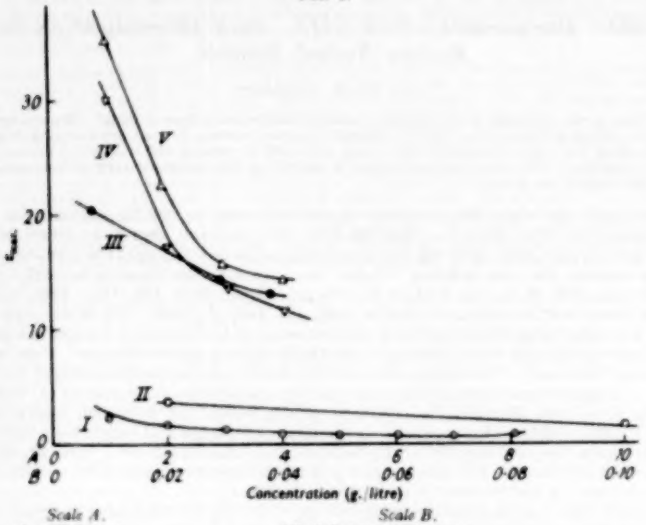
The important rôle which deoxypentose nucleic acids play in the nucleal material of cells (Mirsky *et al.*, *Proc. Nat. Acad. Sci.*, 1942, **28**, 344; *Adv. Enzymol.*, 1943, **3**, 1; Avery, MacLeod, and McCarty, *J. Exp. Med.*, 1944, **79**, 137) necessitates an understanding of the mechanisms of the reactions whereby they are detected. Two of these reactions are those introduced by Dische (*Mikrochemie*, 1930, **8**, 4) and Feulgen (*Z. physiol. Chem.*, 1923, **128**, 154; 1924, **135**, 203). Recently Stacey and his colleagues (*Nature*, 1946, **157**, 740; *J.*, 1949, 1222) reported an explanation of the chemical reactions leading to the formation of the characteristic blue colour shown by deoxyribonucleic acid when subjected to the Dische diphenylamine reaction. They indicated that the reactive moiety of the nucleic acid molecule was its carbohydrate component, 2-deoxy-D-ribose. A detailed examination of this sugar has been described by these authors (*J.*, 1949, 1879, 2836) who have also discussed the specificity of the Dische test (Overend, Shafizadeh, and Stacey, *J.*, 1950, 1027). Measurements on the colours produced in Feulgen tests with nucleic acids have been reported recently by Di Stefano (*Proc. Nat. Acad. Sci.*, 1948, **34**, 75).—The present communication is a continuation of a preliminary report on the chemistry of the Feulgen reaction (Stacey, Li, and Overend, *Nature*, 1949, **163**, 538).

Divergent views exist concerning the deductions to be drawn from results obtained by using the Feulgen test (cf. Danielli, *Symp. Soc. Exp. Biol.*, 1947, **1**, 101; *Quart. J. Microscop. Sci.*, 1949, **90**, 67; Di Stefano, *loc. cit.*; Stedman and Stedman, *Symp. Soc. Exp. Biol.*, 1947, **1**, 232). In part these misunderstandings are due to incomplete evidence about the reactions involved. The general view is that the acid hydrolysis breaks the purine–sugar glycosidic linkage in deoxyribonucleic acid, and that the deoxypentose is then able to exist to some extent in its straight-chain aldehydo-form, and it is in this form that it reacts with Schiff's reagent (*Annalen*, 1866, **140**, 102), forming a reddish compound. This general view contains many assumptions. For example it is assumed that in this test a deoxypentose (*i.e.*, 2-deoxy-D-ribose) would react to some extent at least in its aldehydo-form with Schiff's reagent, and that under the test conditions only the purine bases are cleaved from the nucleic acid. Moreover it is assumed that the colour developed is not due to the deoxypentose partly decomposing in the acid conditions to yield ω-hydroxylævulaldehyde which then reacts with Schiff's reagent to give a soluble dye, subsequently adsorbed on the proteins present in the cell. Stacey *et al.* (*loc. cit.*) showed that this aldehyde was responsible for the development of colour in the Dische diphenylamine test. The decrease in colour intensity in the Feulgen test which results from over-hydrolysis was believed to be caused by some secondary reaction.

The validity of some of these assumptions has been investigated. The intensities of the colours produced by normal hexoses and pentoses and their 2-deoxy-analogues, when Schiff's reagent was added to them, were measured quantitatively. Originally we intended to report our results in graphic form by plotting the wave-length (λ, A.) against the molecular extinction coefficient ($\varepsilon_{max.}$) (Stacey *et al.*, *loc. cit.*), but unfortunately the colour intensities produced were not directly proportional to the concentrations of the solutions. Fig. 1 illustrates the results

obtained when the values of $\epsilon_{max.}$ are plotted against concentration for a series of normal and 2-deoxy-sugars and their derivatives. Consequently we have carried out all our measurements on solutions of the same concentration (*c*, 2·4) and have plotted Spekker readings directly against wave-length. In this way only comparative values of the colour intensities at a certain concentration are obtained, but the results are sufficiently marked to illustrate the subsequent argument. Strict control of the temperature and air contamination is important since both affect the intensities of the colours obtained. It was impossible to reproduce exactly results of Spekker readings with different batches of reagent. The differences between the values obtained for various sugars are however always constant. The comparative measurements shown in Figs. 2 and 3 were carried out with one batch of reagent and those in Figs. 4, 5, and 6 with another.

FIG. 1.



Scale A.
I. D-*Galactose.*
II. D-*Glucose.*
III. 2-*Deoxy*-D-*ribose.*
Scale B.
IV. 2-*Deoxy*-D-*galactose.*
V. 3 : 5 : 6-*Trimethyl* 2-*deoxy*-D-*galactofuranose.*

Fig. 2 shows the results obtained with D-glucose, D-galactose, and D-ribose, and their 2-deoxy-analogues. In all cases the deoxy-sugar shows a much increased intensity of colour compared with its normal analogue. This effect is most pronounced in the hexose series, and it will be observed that 2-deoxy-D-galactose gives a more intense colour than 2-deoxy-D-glucose. In this connection it is noteworthy that other derivatives of D-galactose are known (*e.g.*, 3 : 6-anhydro-D-galactose) which exist predominantly in the aldehydo-form (Haworth, Jackson, and Smith, *J.*, 1940, 620). The sugar component of deoxyribonucleic acid is fixed in its furanose form. This has been proved by Levene and Tipson (*J. Biol. Chem.*, 1935, **109**, 623; *Science*, 1935, **81**, 98) for the thymidine component of the nucleic acid, and more recently for the other deoxyribonucleosides (Todd, private communication). Consequently we investigated next the effect, on the intensity of the colour developed, of preventing the sugar existing in its pyranose form. This was achieved by suitable protection of the hydroxyl group at $C_{(5)}$. Protection by methylation has no effect since D-glucose and its 2 : 3 : 4 : 6-tetramethyl derivative give practically identical Spekker readings (Fig. 3). If the sugars can only exist in furanose or aldehydo-forms, the intensity of colour developed when Schiff's reagent is added, is much enhanced. For example D-glucofuranose 5 : 6-monocarbonate (Haworth and Porter, *J.*, 1929, 2796) and 2-deoxy-D-glucofuranose 5 : 6-monocarbonate (Hughes, Overend, and Stacey, *J.*, 1949, 2846) both show intenser colours than do D-glucose and 2-deoxy-D-glucose when treated according to the procedure described. The most intense colour obtained in the later experiments

was with a sugar which could only exist in its aldehydo-form, namely diethylidene *aldehydo*-L-xylose, and this seems to indicate conclusively that this development of colour is associated with the aldehydo-form. Moreover, unlike other sugars, when the Schiff's reagent was added to this aldehydo-sugar, a quite strong colour developed immediately. In Fig. 4 the results of measurements with various methylated derivatives of 2-deoxy-D-ribose are recorded; of these derivatives 3 : 5-dimethyl 2-deoxy-D-ribofuranose gives the most intense colour with Schiff's reagent. As expected, 3 : 4-dimethyl 2-deoxy-D-ribopyranose gives a slightly less intense colour than 2-deoxy-D-ribose. Fig. 5 shows the results of similar measurements with various derivatives of 2-deoxy-D-galactose. These measurements show clearly that 2-deoxy-sugars give a much more intense colour with Schiff's reagent than do their normal analogues under comparable conditions, an effect enhanced if they are prevented from existing in the pyranose form.

FIG. 2.

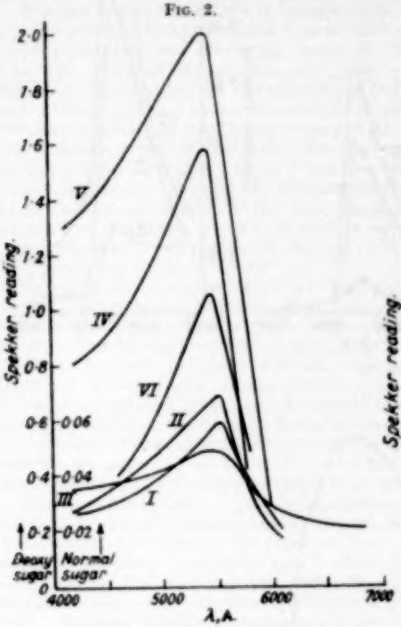


FIG. 3.

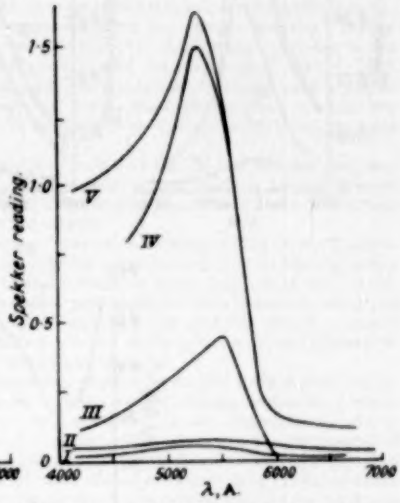


FIG. 2.—*I. Anhydrous* D-*glucose. II.* D-*Galactose. III.* D-*Ribose. IV.* 2-*Deoxy*-D-*glucose. V.* 2-*Deoxy*-D-*galactose. VI.* 2-*Deoxy*-D-*Ribose.*

FIG. 3.—*I.* D-*Glucose. II.* 2 : 3 : 4 : 6-*Tetramethyl*-D-*glucopyranose. III.* D-*Glucofuranose* 5 : 6-*monocarbonate. IV.* 2-*Deoxy*-D-*glucose. V.* 2-*Deoxy*-D-*glucofuranose* 5 : 6-*monocarbonate.*

Finally measurements were carried out on guanosine, a deoxyribonucleotide mixture isolated from the enzymic degradation of deoxyribonucleic acid, probably containing a preponderance of pyrimidine types (Overend and Webb, forthcoming publication), and a purine deoxyribonucleotide; results are shown in Fig. 6. The most intense colour was obtained from the purine deoxyribonucleotide, and this was much more intense than that from guanosine, of which the molecular concentration was much greater.

A consequence of these measurements is that even if the sugar-base glycoside linkages in ribonucleic acid are cleaved during the Feulgen test, the freed reactive group at $C_{(1)}$ of the sugar and Schiff's reagent do not react to give a colour as intense as that which results from similar treatment of deoxyribonucleic acid. Another factor which influences the intensity of the colour developed is the presence of phosphate groups; this is indicated in preliminary experiments and is being further developed.

When the sodium salt of a fibrous sample of deoxyribonucleic acid, isolated from soft herring roe by essentially Mirsky and Pollister's method (*J. Gen. Physiol.*, 1946, **30**, 101), was treated with Schiff's reagent after being kept at pH 2·0 at 100° for 2·75 minutes, it immediately became coloured, and the intensity of the colour became visibly progressively greater. No colour

FIG. 4.

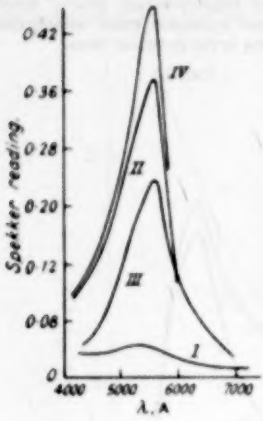


FIG. 5.

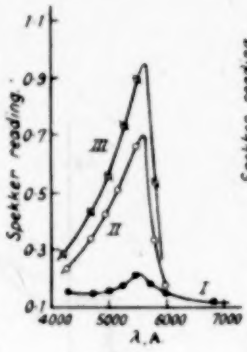


FIG. 6.

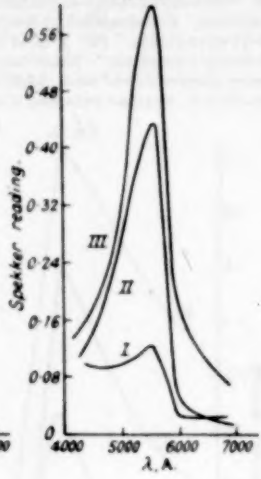


FIG. 7.

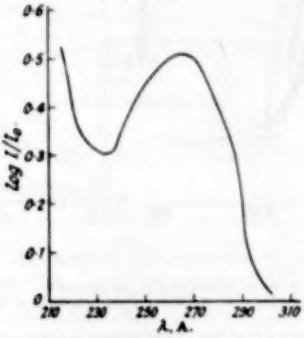


FIG. 4.—D-*Ribose*. *II*. 2-*Deoxy*-D-*ribose*. *III*. 3:4-*Dimethyl* 2-*deoxy*-D-*ribopyranose*. *IV*. 3:5-*Dimethyl* 2-*deoxy*-D-*ribofuranose*.

FIG. 5.—*I*. 2:3:4:6-*Tetramethyl* D-*galactose*. *II*. 3:4:6-*Trimethyl* 2-*deoxy*-D-*galactopyranose*. *III*. 3:5:6-*Trimethyl* 2-*deoxy*-D-*galactofuranose*.

FIG. 6.—*I*. *Guanosine*. *II*. *Pyrimidine deoxyribonucleotide*. *III*. *Purine deoxyribonucleotide*.

could be washed out of the nucleic acid which after being dried was obtained as fine fibres with a violet colour. It seems that in the Feulgen test a reaction occurs between the available reactive group at $C_{(1)}$ of the deoxypentose and the added Schiff's reagent. Wieland and Scheuing (*Ber.*, 1921, **54**, 2527) postulate that in the reaction of a simple aldehyde with Schiff's reagent a complex is formed between two molecules of the aldehyde and the fuchsin–sulphurous acid reagent. That a change of this nature probably occurs is demonstrated by the fact that addition of a simple aldehyde to Schiff's reagent does not merely restore the colour to fuchsin,

but gives a different colour (often violet). It seems that a similar mechanism probably holds for the Feulgen reaction.

A preliminary examination was made of the bases liberated in the Feulgen test. Material passed into solution which showed a strong, broad ultra-violet absorption band with a maximum at 2670 A. ($\log I/I_0 = 0{\cdot}52$; ϵ, 0·82 mg. %) (see Fig. 7). This can be compared with the measurements reported for adenine and guanine, i.e. absorption at 2610 A. ($\log I/I_0 = 1{\cdot}8$; ϵ, 2·2 mg. %) and 2740 A. ($\log I/I_0 = 1{\cdot}0$; ϵ, 2·2 mg. %), respectively. An equimolecular mixture of these purine bases would show in the conditions used an absorption band in the region 2675 A. ($\log. I/I_0 = 0{\cdot}52$; ϵ, 0·82 mg. %). The slight difference in position of the observed and the calculated values may be due to several causes. That hydrolysis of some of the pyrimidine–sugar linkages occurs to a small extent was demonstrated by precipitating some silver salts of pyrimidines from the absorbing solution (cf. Schmidt and Levene, *J. Biol. Chem.*, 1938, **126**, 423).

It is well known that if there is overhydrolysis in the Feulgen test the intensity of the colour is much reduced. Lately renewed interest has been shown in the reasons for this and several explanations have been offered (cf. Bauer, *Z. Zellforsch.*, 1932, **15**, 225; Hillary, *Bot. Gaz.*, 1939, **101**, 276; Di Stefano, *loc. cit.*). The work of Stacey and his co-workers on the properties and reactions of deoxy-pentoses and -hexoses, and in particular of 2-deoxy-D- and -L-ribose, indicates that overhydrolysis of the nucleic acid not only brings it into a more diffusible form but also changes the deoxypentose to some extent into ω-hydroxylævulaldehyde. This aldehyde could be responsible for the results described by various workers. Stacey (*loc. cit.*) tentatively suggested that it was also responsible for the development of colour in the normal Feulgen test, but this was criticized by Danielli (*Symp. Soc. Exptl. Biol.*, 1947, **1**, 101). There is little doubt however that if the time of hydrolysis is extended this compound would be formed, and if washing was not exhaustive it would give a coloured complex when Schiff's reagent was added. This coloured complex could be retained by absorption on to cell proteins (cf. Stedman and Stedman, *loc. cit.*).

Simple preliminary experiments (cf. Experimental) indicated that, in the Feulgen test, any simple aldehyde formed during the hydrolysis procedure could be removed by washing. Hence only a large complex molecule could give the colour with Schiff's reagent, and it is believed that it is the nucleic acid molecule which reacts with the reagent.

From these observations it is possible to obtain some idea of what occurs in the Feulgen reaction. The initial acid hydrolysis results in preferential cleavage of the purine bases from the nucleic acid, although some slight hydrolysis of the pyrimidine bases may also occur. Overhydrolysis results in further degradation of the nucleic acid, and the deoxypentose is converted into ω-hydroxylævulaldehyde and then lævulic acid. Although this aldehyde will give a colour with Schiff's reagent it can be removed from tissues, etc., by washing and so is not responsible for the colour obtained when the Feulgen test is performed correctly.

This does not preclude it from being the compound responsible for the colours obtained by Hillary (*loc. cit.*), as originally suggested by Stacey. In the normal procedure when the purine–sugar linkages are cleaved, the sugar can react to some extent in its aldehydo-form and so combine with Schiff's reagent to give a coloured complex. This effect is probably intensified since in nucleic acids the sugar is present in the furanose form, and it has now been demonstrated that the intensity of colour developed is increased when the sugar cannot exist in the pyranose form. Moreover it has been shown that under similar conditions normal sugars give much less intense colours with Schiff's reagent than do their 2-deoxy-analogues. This fact indicates that the test can be used with reasonable certainty to differentiate between ribo- and deoxyribonucleic acids. Although this has been done in the past, no quantitative data have been put forward to support the results obtained. Since the coloured complex molecule formed is relatively large, the sites exhibiting the Feulgen colour are unlikely to be found in the cell far removed from the locations of the deoxyribonucleic acid. It is realised that the ideas proposed represent somewhat ideal conditions in that they apply only to nucleic acids. It is conceivable that other materials occur in cells which could give a colour with Schiff's reagent. Moreover the Feulgen reaction is carried out in cells in the presence of proteins and it is likely that these influence to some extent the formation of colour (cf. Hamazaki, *Nissin Igaku, Tokyo*, 1939, **28**, 46). However as applied to nucleic acids, the mechanism described could account for the development of colour when the Feulgen reaction is correctly performed.

Experimental.

Investigation of the Colours produced by Adding Schiff's Reagent to Certain Sugars.—The intensities of the colours produced by normal hexoses and pentoses and their 2-deoxy-analogues when Schiff's reagent was added to them, were measured quantitatively. The Schiff's reagent used for all the measurements

was the supersensitive aldehyde reagent introduced by Tobie (*Ind. Eng. Chem. Anal.*, 1942, **14**, 405) for the demonstration of free aldehyde groups in certain aldoses. Trial experiments indicated that it gave a negative reaction with ketoses and glycosides. The reagent was stored in a well-stoppered, dark bottle in a cool place. The normal pentoses and hexoses used were commercial samples, purified by repeated recrystallisation, and the deoxy-pentoses and -hexoses and their derivatives were prepared according to the methods of Stacey *et al.* (*J.*, 1949, 1358, 1879, 2836, 2841, 2846). The colours developed were measured in a Spekker photoelectric absorptiometer with Ilford filters 601—608 (λ = 4300—6900 A.) All the measurements except where otherwise indicated were obtained by dissolving the appropriate sugar (0·012 g.) in distilled water (4 ml.) followed by the addition of the standard Schiff's reagent (1 ml.). After the solution had been warmed at 35° for 1 minute the tube was well plugged, cooled rapidly to 17°, and kept at this temperature for 1·25 hours. The intensity of the colour developed was then measured. Results are shown in Figs. 1—5.

Investigation of the Colours produced by adding Schiff's Reagent to a Nucleoside and Some Nucleotides.—The compounds used were guanosine [prepared according to Bredereck, Richter, and Martini (*Ber.*, 1941, **74**, 694)], a deoxyribonucleotide mixture isolated from the enzymic degradation of thymonucleic acid and probably containing a preponderance of the pyrimidine types (Overend and Webb, forthcoming publication), and a purine deoxyribonucleotide kindly supplied by Dr. Chong Fu-Li (late of this Department). The experiments were conducted according to the Widström modification (*Biochem. Z.*, 1928, **199**, 298) of the Feulgen reaction. The materials (0·012 g. of each) were heated separately at 100° for exactly 2·75 minutes in a citrate buffer (pH 2·0; 2 ml.) (cf. Deriaz *et al.*, *J.*, 1949, 1222). After the solution had cooled, distilled water (2 ml.) and standard Schiff's reagent (1 ml.) were added, and the procedure described above followed. Results are shown in Fig. 6.

Treatment of a Partly Hydrolysed Deoxyribonucleic Acid with Schiff's Reagent.—The sodium salt of a fibrous sample of deoxyribonucleic acid isolated from soft herring roe essentially by Mirsky and Pollister's method (*J. Gen. Physiol.*, 1946, **30**, 101) was treated with a citrate buffer (pH 2·0) and 100° for 2·75 minutes. The resulting solution was cooled to 0°. Polymeric material still in solution was precipitated by addition of ethanol (cf. Gulland, Jordan, and Threlfall, *J.*, 1947, 1129), and the precipitate was collected by centrifugation, washed repeatedly with physiological saline and water, and collected by centrifugation. Control experiments indicated that this washing procedure was sufficient to remove any adsorbed aldehydes of low molecular weight, such as ω-hydroxylævulaldehyde. Schiff's reagent was added to an aqueous suspension of the white polymeric material isolated, and this immediately became violet, the intensity of the colour visibly becoming progressively greater. Although it contained excess of Schiff's reagent the supernatant liquid remained colourless even after 48 hours. It was removed by decantation and the coloured complex formed by the combination of the partly hydrolysed nucleic acid and Schiff's reagent was washed with water. No colour could be washed out of it. After being dried, the solid was obtained as fine violet fibres. The colour was light fast for several weeks.

Investigation of the Bases liberated During Mild Acidic Hydrolysis of Deoxyribonucleic Acid.—Fibrous deoxyribonucleic acid (0·0876 g.) and dilute sulphuric acid (0·5N.; 2 c.c.) were heated at 100° for 2·75 minutes. Addition of ethanol (excess) and physiological saline yielded a precipitate (*A*) which was removed and washed by centrifugation. The washings were added to the mother-liquors, giving a total volume of 7 ml. Ultra-violet absorption measurements on this showed a strong broad band at 2670 A. ($\log I/I_0 = 0·52$; c, 0·82 mg. %) (see Fig. 7) [cf. adenine and guanine which absorb at 2610 A. ($\log I/I_0 = 1·8$; c, 2·2 mg. %) and 2740 A. ($\log I/I_0 = 1·0$; c, 2·2 mg. %), respectively].

The mother liquor (1 ml.) was treated with a saturated solution of silver sulphate (2 ml.). A precipitate of the silver salts of guanine and adenine was formed (Schmidt and Levene, *J. Biol. Chem.*, 1938, **126**, 423). After cooling to 0° for 0·5 hour, the precipitate was separated by centrifugation and washed twice, by stirring at 0° with a saturated solution of silver sulphate followed by centrifugation. The solution was combined with the washings and analysed for pyrimidine nitrogen [Found: N(pyrimidine), 2·0%].

The precipitated polymeric material (*A*) was shown readily to develop a colour when excess of Schiff's reagent was added, and its general behaviour was identical with that of the material obtained in the previous experiment.

Effect of a Simple Aldehyde.—Deoxyribonucleoprotein from soft herring roe, isolated as described above, and the protein stripped from it were separately soaked in N-butyraldehyde for 1·5 hours. The proteins were then washed repeatedly (15 times) by being centrifuged with water containing a trace of ethanol (distilled over solid sodium hydroxide). After this treatment excess of Schiff's reagent was added to the solids. Neither developed colour, nor did the reagent. Next a coloured solution was prepared by adding Schiff's reagent (5 c.c.) to N-butyraldehyde (2 drops). The nucleoprotein and stripped protein were separately soaked in it for 1·5 hours, and then washed by being centrifuged ten times with water. Both had strongly adsorbed the dye which was not removed by being washed with water. The stripped protein was steeped in undeveloped Schiff's reagent for 1·5 hours, and then repeatedly washed by being centrifuged with water. On addition of N-butyraldehyde to the washed solid, suspended in water, and shaking the suspension it became coloured showing that it adsorbed the undeveloped reagent.

The author is indebted to Professor M. Stacey, F.R.S., for suggesting this topic and for his interest in the work. He also thanks the Board of the British Rubber Producers' Research Association for financial assistance which enabled him to undertake this investigation. Thanks are due to Dr. E. J. Bourne for kindly supplying a sample of diethylidene *aldehydo*-D-xylose.

CHEMISTRY DEPARTMENT,
THE UNIVERSITY, BIRMINGHAM.

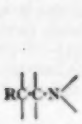
[*Received, April 25th*, 1950.]

534. *New 5-Aminoglyoxalines as Potential Adrenergic Agents.*

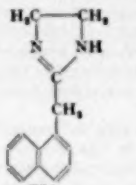
By H. Bader, J. D. Downer, and (Mrs.) P. Driver.

The preparation of a number of 5-aminoglyoxaline hydrochlorides containing part of the 2-substituted ethylamine structure in the hetero-ring is described. A novel application of the Mannich reaction to the glyoxaline ring is also described, and a discussion on ultra-violet absorption spectra of the 5-aminoglyoxalines is given. The compounds are to be tested for sympathomimetic activity.

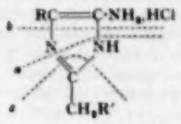
With the exception of the carbonic acid derivatives for which "pressor effects" have been claimed (Fastier, *Nature*, 1944, **154**, 429), compounds endowed with a true adrenergic or sympathomimetic action all appear to possess a strongly basic character and the fundamental structure (I) where R is an alkyl, aromatic, or heterocyclic radical.



(I.)



(II.)



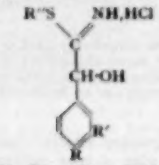
(III.)

The aim of the present work is to find new drugs in this field possessing comparable activity to that of adrenaline and related compounds but without their instability and associated undesirable side activities. It appeared to us that the most promising development might be the introduction of new ring systems in the basic structures, which incorporate the nitrogen atom in the ring. This development has already been successful in the employment of the dihydroglyoxaline ring [*e.g.*, Privine (II), which is now used clinically in peripheral vascular disorders] (Hartmann and Isler, *Arch. Exp. Path. Pharm.*, 1939, **192**, 141; Scholz, *Ind. Eng. Chem.*, 1945, **37**, 120).

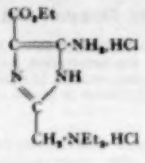
This communication describes the preparation of a number of potential pressor amines of the type (III) with the nitrogen atoms of the basic structure (I) contained in a glyoxaline ring. The 5-aminoglyoxalines have been chosen because, unlike glyoxalines in general, which are conspicuously stable to degradative reagents, they are on the whole easily broken down under acid conditions. Existing information (Fargher and Pyman, *J.*, 1919, **115**, 217; Fargher, *J.*, 1920, **117**, 668; Grant and Pyman, *J.*, 1921, **119**, 1893; Pyman, *J.*, 1922, **121**, 2616; Balaban, *J.*, 1930, 268) suggests that the fission may proceed in three ways (III; *a*, *b*, or *c*). Fission (*a*) is the more usual and is thought to proceed through the ketodihydroglyoxaline. The other degradations (*b*) and (*c*) are more conspicuous where R is electropositive, *e.g.*, Me (Pyman, *loc. cit.*). The fission (*a*) or (*b*) if occurring in glyoxalines of structure (III) would still preserve the basic skeleton (I) of adrenergic drugs. In the main, therefore, 2-substituted 5-amino-4-phenyl(or carbethoxy)glyoxalines (type III) have been prepared. The effect of substituents in the basic structure (I) on the physiological activity is fully reviewed elsewhere (Hartmann and Isler, *loc. cit.*; Hartung, *Chem. Reviews*, 1931, **9**, 389; Rajagopalan, *Current Sci.*, 1945, **14**, 56) and has been used in selecting the substituents R′ in (III). Many of the 5-aminoglyoxalines prepared, such as [III; R = CO_2Et, R′ = Ph; R = Ph, R′ = 3 : 4 : 5-$C_6H_2(OMe)_3$; and R = H, R′ = β-$C_{10}H_7$], will, therefore, be found to contain substituents analogous to the aryl substituents in known effective adrenergic agents.

The 5-aminoglyoxaline hydrochlorides (III; R = CO_2Et or Ph; R′ = phenyl, *m*- or *p*-substituted phenyl, α- or β-$C_{10}H_7$) were prepared by the method of Cook, Davis, Heilbron, and Thomas (*J.*, 1949, 1071) by condensing ethyl α-aminocyanoacetate or α-aminobenzyl cyanide with the appropriate thio-iminoether hydrochloride in boiling chloroform. This reaction proceeded smoothly in most cases to give excellent yields. In a few cases yields were much reduced owing to the reverse condensation taking prominence with the formation of ammonium chloride and presumably the *N*-substituted thio-iminoether (Abraham, Baker, Barltrop, Chain, King, Robinson, and Waley, CPS. 549). This was most noticeable in attempts to condense the thio-iminoethers (IV; R = R′ = H, R = OMe, R′ = H) with ethyl α-aminocyanoacetate

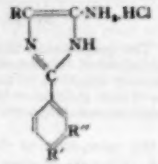
and the thio-iminoether (IV; RR′ = OCH_2O) with α-aminobenzyl cyanide, in which the required glyoxalines could not be isolated.



(IV; R″ = Et or CH_2Ph)



(V.)



(VI.)

In many cases, occurring only when α-aminobenzyl cyanide was used as one of the reactants, an abnormally long period of refluxing was necessary for a good yield of glyoxaline (see Table III). When only the usual time of refluxing was given, besides a poor yield of glyoxaline, α-aminobenzyl cyanide hydrochloride was isolated. In this connection it was shown that α-aminobenzyl cyanide hydrochloride reacts slowly with *p*-nitrophenylacetimino benzyl thioether base to give the required glyoxaline. When, however, the reaction between α-aminobenzyl cyanide and thio-iminoether hydrochlorides was performed in the presence of an excess of hydrogen chloride, no glyoxalines could be isolated.

Condensation of α-aminopropionitrile with thio-iminoether hydrochlorides from substituted benzyl cyanides invariably proceeded in the reverse direction. With benzimino benzyl thioether hydrochloride, however, the expected 5-amino-2-phenyl-4-methylglyoxaline hydrochloride was obtained. When aminoacetonitrile reacted with thio-iminoether hydrochlorides under the usual conditions, its hydrochloride was precipitated and failed to react further. This was overcome by performing the reaction at room temperature in the presence of one equivalent of pyridine, the glyoxalines (*e.g.*, III; R = H, R′ = β-$C_{10}H_7$) then being obtained. These last two α-amino-nitriles have not previously been employed in the thio-iminoether–α-amino-nitrile synthesis of glyoxalines.

Reduction of the glyoxalines (III; R = CO_2Et or Ph, R′ = *p*- or *m*-$NO_2{\cdot}C_6H_4$) with stannous chloride in hydrochloric acid readily gave the corresponding amino-derivatives.

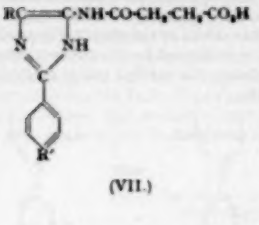
Refluxing of 5-amino-4-carbethoxyglyoxaline, trioxymethylene, and diethylamine in ethanol gave a good yield of 5-amino-4-carbethoxy-2-diethylaminomethylglyoxaline dihydrochloride (V). Only in a few isolated cases has the Mannich reaction been applied to azole rings, and in particular the thiazole ring (Albertson, *J. Amer. Chem. Soc.*, 1948, **70**, 669). Reactions are known, however, where 1-alkyl- and 1-aralkyl-glyoxalines have been condensed with formaldehyde to give 2-hydroxymethylglyoxalines (*e.g.*, Sarisin, *Helv. Chim. Acta*, 1923, **6**, 377; Sonn *et al.*, *Ber.*, 1924, **57**, 953; Grindley and Pyman, *J.*, 1927, 3128; Jones, *J. Amer. Chem. Soc.*, 1949, **71**, 383). In the present case, the 4- and 5-positions being occupied, condensation has occurred in the 2-position, as proved by an alternative synthesis of (V) from diethylaminoacetonitrile by the general method.

Since glyoxaline itself has pressor activity (Fastier, *Brit. J. Pharmacol.*, 1948, **3**, 198; Fastier and Reid, *ibid.*, p. 205), and moreover the 5-amino-group introduces an additional amidino-grouping, it was considered possible that the 5-aminoglyoxaline moiety itself might possess pressor activity, especially in the case of the 4-phenyl derivatives which contain a hidden 2-phenylethylamine structure. This possibility was examined by preparing a number of glyoxalines of the type (VI; R = Me, Ph, or CO_2Et; R′ = H, Cl, NO_2, or NH_2; R″ = H; R′ = R″ = OMe). These were found to possess little or no activity but were surprisingly non-toxic. They were all strongly fluorescent in solution. Succinyl derivatives (VII) in place of the more insoluble glyoxaline hydrochlorides were prepared.

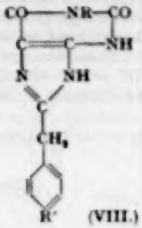
In order to investigate the effect of the introduction of a pyrimidine ring on physiological activity, the purines (VIII; R = Me, R′ = NO_2 or $NH_2{\cdot}HCl$; R = Ph, R′ = H) have been prepared by ring closure of the appropriate 5-ureido-4-carbethoxyglyoxalines according to the method of Cook, Heilbron, Macdonald, and Mahadevan (*J.*, 1949, 1064).

In the aliphatic amines effective pressor activity is found in members with a chain of 6—8 carbon atoms (Rohrmann and Shonle, *J. Amer. Chem. Soc.*, 1944, **66**, 1516). This prompted the preparation of 5-amino-4-phenyl-2-*n*-heptylglyoxaline hydrochloride from *n*-amyl cyanide and the bisiminazole (IX) from sebaconitrile *via* the bisthio-iminoether hydrochloride. The latter might also be expected to exhibit trypanocidal activity (see King, Lourie, and Yorke, *Lancet*, 1937, **233**, 1360; *Ann. Trop. Med. Parasit.*, 1938, **32**, 177).

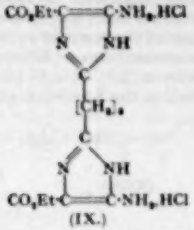
The biological results will be published elsewhere.



(VII.)



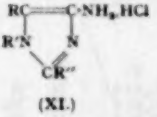
(VIII.)



(IX.)

Light-absorption Properties of 5-Aminoglyoxalines.—With a view to assess the influence of substitution in the glyoxaline ring, the ultra-violet light absorption of many of the compounds described in this paper has been determined. The results are collected in Table I. They will be seen to agree with the generally accepted basic structure (X) deduced from chemical evidence (Cook, Heilbron, *et al.*, Studies in the Azole Series, *J.*, 1948—1949). The glyoxaline hydro-

(X.)



(XI.)

chlorides (XI; R = H, CO_2Et, or Ph; R′ = H or Me; R″ = H, Me, or aralkyl) exhibit a wide absorption band, in general of high intensity and with a maximum in the 2650—2850-A. region. With regard to the effect of substitution in the 4-position in the unsubstituted glyoxaline (XI; R = R′ = H; R″ = *p*-$NO_2{\cdot}C_6H_4{\cdot}CH_2$), the absorption curves (Fig. 1) of the corresponding 4-carbethoxy- or 4-phenyl- compounds are essentially similar but are shifted by some 100 and

FIG. 1.

Absorption curves showing effect of 4-substituent.

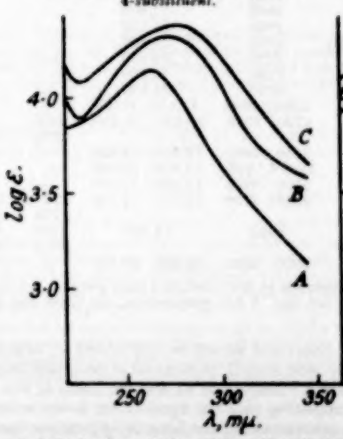


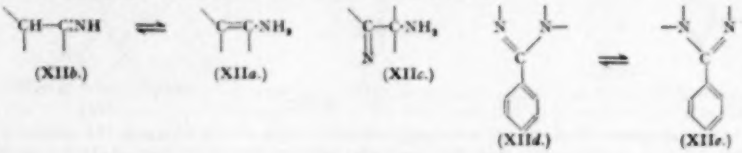
FIG. 2.

Absorption curves showing effect of acidification.

FIG. 1.—*A. 5-Amino-2-p-nitrobenzylglyoxaline hydrochloride. B. 5-Amino-2-p-nitrobenzyl-4-carbethoxy glyoxaline hydrochloride. C. 5-Amino-2-p-nitrobenzyl-4-phenylglyoxaline hydrochloride.*

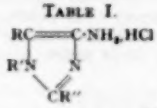
FIG. 2.—*A. 5-Amino-4-carbethoxy-2-phenylglyoxaline. B. 5-Amino-4-carbethoxy-2-phenylglyoxaline hydrochloride. C. 5-Amino-4-carbethoxy-2-phenyl-3-methylglyoxaline. D. 5-Amino-4-carbethoxy-2-phenyl-3-methylglyoxaline hydrochloride.*

130 A. respectively to longer wave-lengths and possess higher maximum intensity. This is in accordance with the basic structure (X), both bathochromic and hyperchromic shifts resulting from the extra conjugation of a CO_2Et or Ph group attached directly to the heterocyclic ring. It implies the presence in the ring of a double bond on the 4-carbon atom as existing in the partial tautomeric forms (XIIa) and XIIc). The existence of (XIIa) is confirmed by the ready methylation of (XI; R = CO_2Et, R′ = H, R″ = Ph) with diazomethane, the methyl group attaching itself to the 3-nitrogen atom (Cook and Thomas, *J.*, 1950, 1884).



(XIIb.) (XIIa.) (XIIc.) (XIId.) (XIIe.)

TABLE I.



No.	R.	R′.	R″.	Hydrochloride. $\lambda_{max.}$, A.[a]	Hydrochloride. ε.	Base. $\lambda_{max.}$, A.[a]	Base. ε.
1	CO_2Et [b,c]	H	H	2740	14,450	—	—
2	CO_2Et [c]	H	Me	2730	17,200	—	—
3	CO_2Et [b]	Me	Me	2705	12,750	2810	13,650
4	H	H	*p*-NO_2·C_6H_4·CH_3	2640	14,000	—	—
5	H	H	β-$C_{10}H_7$·CH_3	2660	6,600	—	—
6	Ph	H	α-$C_{10}H_7$·CH_3	2875	21,150	—	—
7	Ph	H	β-$C_{10}H_7$·CH_3	2800	21,150	—	—
8	Ph	H	*p*-NO_2·C_6H_4·CH_3	2770	23,450	—	—
9	Ph	H	*p*-Cl·C_6H_4·CH_3	2810	12,600	—	—
10	Ph	H	CH_3·C_6H_4·NH_2,HCl (*p*)	2800	15,150	—	—
11	Ph	H	*p*-OH·C_6H_4·CH_3	2835	19,500	—	—
12	Ph	H	*m*-NO_2·C_6H_4·CH_3	2700	15,400	—	—
13	Ph	H	CH_3·C_6H_4·NH_2,HCl(*m*)	2835	10,550	—	—
14	Ph	H	*m*-OH·C_6H_4·CH_3	2810	17,000	—	—
15	Ph	H	3 : 4-$(OMe)_2C_6H_3$·CH_3	2830	20,150	—	—
16	Ph	H	3 : 4 : 5-$(OMe)_3C_6H_2$·CH_3	2810	15,900	—	—
17	Ph	H	3 : 4-$(O_2CH_2)C_6H_3$·CH_3	2870	14,650	—	—
18	CO_2Et	H	Ph·CH_3	2730	14,900	—	—
19	CO_2Et	H	*p*-NO_2·C_6H_4·CH_3	2745	21,150	—	—
20	CO_2Et	H	CH_3·NEt_2,HCl	2795; 2395	11,100; 6,100	—	—
21	Ph	H	Ph	2760; 3380	10,400; 17,400	2330; 3370	9,000; 13,900
22	Ph	H	*p*-Cl·C_6H_4	2345; 3460	13,500; 18,050	—	—
23	Ph	H	3 : 4-$(OMe)_2C_6H_3$	2790 [a]; 3360	10,550; 23,600	—	—
24	CO_2Et	H	*p*-NO_2·C_6H_4	2700; 3900	12,450; 13,150	—	—
25	CO_2Et	H	Ph	2310; 3170	13,050; 14,150	2365; 3175	17,400; 16,400
26	CO_2Et [b,d]	Me	Ph	2960	13,500	2325; 3050	15,150; 12,900
27	CO_2Et	H	3 : 4-$(OMe)_2C_6H_3$	2555; 3250	12,400; 20,400	—	—

[a] Inflexion. [b] The preparation of these compounds is described in a later paper. [c] For preparation, see Cook, Davis, Heilbron, and Thomas, *loc. cit.* [d] For preparation, see Cook and Thomas, *loc. cit.* [e] Ethanol was used as solvent.

Structure (XIIb) can exist only in the free bases and should be eliminated by acidification. If it does exist in the free base a hypsochromic shift should be detectable on acidification. In the case of glyoxalines unsubstituted in position 3 (compounds 21 and 25, Table I) the spectra are not appreciably shifted on acidification, suggesting that the equilibrium is not in favour of the form (XIIb) (Fig. 2). On the other hand, comparison of the 3-methylglyoxaline bases with their hydrochlorides (compounds 3 and 26, Table I) reveals the existence of a hypsochromic effect of *ca.* 100 A. in each case showing a definite contribution of the (XIIb) form to their resonance equilibrium (Fig. 2).

Introduction of a methyl or aralkyl group in the 2-position of (XI; R = CO_2Et, R′ = R″ =

H) does not alter sensibly the position or intensity of the light-absorption maximum. With aryl substituents in the 2-position, however (compounds 25 and 27, Table I), the maximum is shifted some 600 A. to longer wave-lengths (Fig. 3). This again agrees with the basic structure resulting from the extra conjugating of an aryl group (attached directly to the heterocyclic ring) right through to the 4-carbethoxy-group. In addition the absorption curves of the 2 arylglyoxalines exhibit a fine structure in the 2350—2550 A. region. Again with 2-aryl-4-phenylglyoxaline hydrochlorides (compounds 21 to 23, Table I) the same effect is noticed and the bathochromic shift is even greater. This effect, therefore, agrees with the presence in the ring of a double bond on the 2-carbon atom as in the partial structures (XII*d*) and (XII*e*).

FIG. 3.

Absorption curves showing effect of 2-substituent.

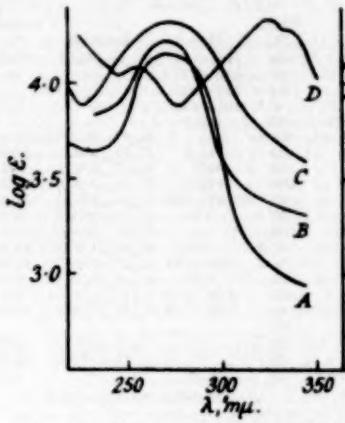


FIG. 4.

Absorption curves showing effect of 3-methyl substitution.

FIG. 3.—*A. 5-Amino-4-carbethoxyglyoxaline hydrochloride. B. 5-Amino-4-carbethoxy-2-methylglyoxaline hydrochloride. C. 5-Amino-4-carbethoxy-2-p-nitrobenzylglyoxaline hydrochloride. D. 5-Amino-4-carbethoxy-2-(3′ : 4′-dimethoxyphenyl)glyoxaline hydrochloride.*

FIG. 4.—*A. 5-Amino-4-carbethoxy-2-phenylglyoxaline. B. 5-Amino-4-carbethoxy-2-phenyl-3-methylglyoxaline.*

Methylation of the nitrogen in the 3-position (*e.g.*, compound 26) eliminates the partial structures (XII*c*) and (XII*d*) which account for the hypsochromic shift (Fig. 4) of 120 A.

EXPERIMENTAL.

(M. p.s are uncorrected. Analyses are by Drs. Weiler and Strauss.)

Nitriles.—The preparation of the required nitriles according to methods described in the literature, in the main, presented no difficulty. The following observations are made. Purification of the crude *p*-nitrobenzonitrile–copper salt complex, prepared by Sandmeyer reaction on *p*-nitroaniline (Bogert and Kohnstamm, *J. Amer. Chem. Soc.*, 1903, **25**, 479), was facilitated by Soxhlet extraction with carbon tetrachloride, giving a yield of 75%; m. p. 146°.

m-Nitrobenzyl alcohol (required for the *m*-substituted benzyl cyanides) was prepared in improved yield (83%) [b. p. 166—169°/0·3—1·5 mm., n_D^{25} 1·5760 (see Ferrier, *Compt. rend.*, 1945, **220**, 460)] by reduction of *m*-nitrobenzaldehyde (500 g.) with aluminium *iso*propoxide (116 g.) and dry *iso*propyl alcohol (7 l.) with distillation of the acetone as it is formed through a Dufton column at *ca.* 60 drops/minutes for 24 hours. Concentration *in vacuo* to 1 l., acidification with a mixture of concentrated hydrochloric acid (320 c.c.) and water (2·4 l.), and extraction with ether gave the alcohol on distillation.

m-Nitrobenzyl cyanide is not adequately described nor is its b. p. given in the literature. It was prepared as follows: Potassium cyanide (121·6 g.) in ethanol (130 c.c.) and water (250 c.c.) was added to a boiling solution of *m*-nitrobenzyl chloride (321 g.) (from the alcohol by the method of Norris and Taylor, *J. Amer. Chem. Soc.*, 1924, **46**, 755) in ethanol (1·5 l.). The resulting mixture was refluxed for 3 hours and concentrated to 500 c.c. *in vacuo*. Addition of water (1 l.), extraction with ether (700 c.c.), and distillation *in vacuo* gave yellow needles of *m*-nitrobenzyl cyanide (256 g., 84·5%), b. p. 180°/1·5 mm.

Thio-iminoether Hydrochlorides.—The following general method, essentially that of Pinner ("Die Imido Ether"), was employed for their preparation: Dry hydrogen chloride was passed into a mixture of the nitrile (1 mol.) and the thiol (1—2 mols.) at 0—5° until 1·1 mols. of hydrogen chloride had been absorbed. (In most cases a diluent, chloroform or ether, was employed to effect dissolution of the nitrile or aid subsequent filtration.) The resultant product was then kept for 1—10 days at 0° until the thio-iminoether hydrochloride separated. Most of these hydrochlorides are new, and where possible they have been titrated against standard alkali and in nearly all cases characterised by their m. p. In some cases, however, the thio-iminoether hydrochloride failed to crystallise (usually when chloroform was employed) or separated as a gum. In these cases either the excess of hydrochloric acid was removed *in vacuo* and the chloroform solution used as such, or the diluent was completely removed, leaving a somewhat crude product which was employed in the condensation. The data, therefore, for the thio-iminoether hydrochlorides prepared as summarised in Table II are not complete.

TABLE II.

Thio-iminoether hydrochlorides, R'S·CR:NH,HCl.

R.	R'	Solvent.	Yield, %	M. p.†	Formula.	HCl: Found, %	HCl: Req., %
Ph	CH_2Ph	(Nil)	94	172—174° †	$C_{14}H_{14}NSCl$	12·55	13·85
p-$NO_2C_6H_4$	CH_2Ph	Et_2O	60	166—170 †	—	—	—
p-ClC_6H_4	CH_2Ph	"	64	180—181	—	—	—
3 : 4-$(OMe)_2C_6H_3$	CH_2Ph	"	5 *	191—193	—	—	—
3 : 4-$(OMe)_2C_6H_3$	Et	Excess EtSH	94	190 †	—	—	—
p-OAc·C_6H_4	CH_2Ph	$CHCl_3$	63·8	215	$C_{16}H_{16}O_2NSCl$	11·4	11·35
CH_2Ph	CH_2Ph	(Nil)	69	141 †	$C_{15}H_{14}NSCl$	13·25	13·15
CH_2Ph	Et	Et_2O	63	117	$C_{10}H_{14}NSCl$	16·1	16·9
p-$NO_2C_6H_4$·CH_2	CH_2Ph	$CHCl_3$	100	174 †	$C_{15}H_{13}O_2N_2SCl$	11·35	11·30
p-ClC_6H_4·CH_2	CH_2Ph	Et_2O	62	155—156	$C_{15}H_{13}NSCl_2$	11·35	11·70
p-OH·C_6H_4·CH_2	Et	"	96	171	$C_{10}H_{15}ONSCl$	15·75	15·75
p-OMe·C_6H_4·CH_2	CH_2Ph	Et_2O–$CHCl_3$	100	—	$C_{16}H_{16}ONSCl$	12·3	11·9
m-$NO_2C_6H_4$·CH_2	Et	"	81·8	142	$C_{10}H_{13}O_2N_2SCl$	14·05	14·0
m-OH·C_6H_4·CH_2	Et	"	76·2	152—153	$C_{10}H_{15}ONSCl$	15·3	16·3
3 : 4-$(OMe)_2C_6H_3$·CH_2	Et	$CHCl_3$	49	163	$C_{13}H_{19}O_2NSCl$	13·9	13·2
3 : 4 : 5-$(OMe)_3C_6H_2$·CH_2	CH_2Ph	"	61	140—145	$C_{19}H_{24}O_3NSCl$	9·6	9·9
3 : 4-(O_2CH_2):C_6H_3·CH_2	CH_2Ph	Et_2O	64	123—125	$C_{16}H_{16}O_2NSCl$	11·35	11·35
α-$C_{10}H_7$·CH_2	Et	$CHCl_3$	90	—	—	—	—
β-$C_{10}H_7$·CH_2	Et	Et_2O	66	—	$C_{14}H_{14}NSCl$	14·05	13·8
Ph·CH(OH)	CH_2Ph	"	58	—	$C_{15}H_{14}ONSCl$	13·15	12·4
Bis-compound –$[CH_2]_5$–	Et	$CHCl_3$ or Et_2O	90	*ca.* 80	—	—	—

* After 36 hours. † With decomposition.

The *glyoxaline hydrochlorides* summarised in Table III were prepared by the following general method, essentially that of Cook, Davis, Heilbron, and Thomas (*loc. cit.*). The thio-iminoether hydrochloride (1 mol.), the α-amino-nitrile (1 mol.), and chloroform (10 mols.) were mixed, usually giving a clear solution, and refluxed for 1—2 hours (unless otherwise stated), and the glyoxaline hydrochloride which separated was collected. They could all be diazotised, the diazonium solutions giving red dyes with sodium β-naphthoxide. With aldehydes they produced coloured Schiff's bases. They were soluble to difficultly soluble in water according to substituents, the addition of alkalis precipitating the bases. They were soluble to difficultly soluble in hot methanol and ethanol but usually insoluble in other organic solvents.

A mixture of *p*-nitrophenylacetimino benzyl thioether hydrochloride (1·5 g.) and anhydrous potassium carbonate (0·41 g., 1 mol.) was mixed into a paste with chloroform. The volume was adjusted to 20 c.c. with chloroform, α-aminobenzyl cyanide hydrochloride (0·75 g.) added, and the mixture refluxed for several hours. The cold crude product was filtered off, ground with water, filtered off, and washed with water. The dried crude solid (0·4 g.), m. p. 220—222° (decomp.), was crystallised from methanol, giving pale lemon-coloured needles of 5-amino-2-*p*-nitrobenzyl-4-phenylglyoxaline hydrochloride, m. p. and mixed m. p. 232° (decomp.).

Glyoxaline Bases.—5-Amino-2 : 4-diphenylglyoxaline hydrochloride (12 g.) was triturated with 3N-sodium carbonate (excess), diluted with water, warmed to 50°, and filtered to give the crude base (9 g.) which crystallised from benzene in prismatic needles of *5-amino-2 : 4-diphenylglyoxaline*, m. p. 165° (Found: C, 76·3; H, 5·5; N, 17·6. $C_{15}H_{13}N_3$ requires C, 76·55; H, 5·55; N, 17·9%). It was very soluble in methanol, ethanol, and ethyl acetate. The crude *base* (4·5 g.) was precipitated when a lukewarm solution of 5-amino-4-carbethoxy-2-(3 : 4-dimethoxyphenyl)glyoxaline hydrochloride (6 g.) in water (250 c.c.) was neutralised with 3N-sodium carbonate; it crystallised from ethyl acetate in colourless prisms, m. p. 198° (Found: C, 57·5; H, 5·4; N, 14·4. $C_{14}H_{17}O_4N_3$ required C, 57·7; H, 5·9; N, 14·4%).

Neutralisation of a solution of 5-amino-4-phenyl-2-*p*-chlorophenylglyoxaline hydrochloride (10 g.) in boiling water (2 l.) with 3N-sodium carbonate gave the crude *base*, which crystallised from aqueous methanol in greenish-yellow prisms (6·5 g.), m. p. 286—290° (decomp.) (Found: C, 66·5; H, 4·7; N, 15·7. $C_{15}H_{12}N_3Cl$ requires C, 66·8; H, 4·5; N, 15·6%). Its solution in methanol, ethanol, or ethyl acetate had a green fluorescence. Similarly, the crude *base* (4 g.) from 5-amino-4-carbethoxy-2-phenyl-

glyoxaline hydrochloride crystallised from aqueous ethanol in colourless prisms, m. p. 219° (decomp.) (Found : C, 62·2; H, 5·8. $C_{11}H_{14}O_3N_2$ requires C, 62·3; H, 5·7%).

Refluxing of 5-amino-4-carbethoxy-2-*p*-nitrophenylglyoxaline hydrochloride (7 g.) with methyl *iso*thiocyanate (4·5 c.c.) in pyridine (60 c.c.) for 1 hour failed to give the methylthioureido-derivative. Instead, the unaltered *base* (4·4 g.), m. p. >280° (decomp.) (Found : C, 52·7; H, 4·55; N, 20·5. $C_{13}H_{13}O_3N_4$ requires C, 52·2; H, 4·4; N, 20·3%), crystallised from the pyridine liquor in colourless small prisms. It was insoluble in water and common organic solvents.

Succinyl Derivatives.—5-Amino-4-phenyl-2-*p*-nitrophenylglyoxaline hydrochloride (6 g.) was refluxed in pyridine (40 c.c.) with succinic anhydride (3·3 g.) for 1 hour. The thick syrup obtained on evaporation *in vacuo* was crystallised from aqueous ethanol give golden-yellow hair-like needles of *5-(β-carboxypropionamido)-4-phenyl-2-p-nitrophenylglyoxaline* (3·5 g.), m. p. >300° (Found : N, 15·0. $C_{19}H_{14}O_6N_4$ requires N, 14·75%). It was soluble in dilute aqueous sodium hydrogen carbonate.

Refluxing of a suspension of 5-amino-4-phenyl-2-*p*-chlorophenylglyoxaline (4 g.) in benzene (70 c.c.) with succinic anhydride (2 g.) for 30 minutes and crystallisation of the crude product (5·5 g.) from aqueous ethanol gave pale greenish-yellow needles of *5-(β-carboxypropionamido)-4-phenyl-2-p-chlorophenylglyoxaline*, m. p. 223° (decomp.) (Found : C, 61·5; H, 4·6; N, 11·2. $C_{19}H_{15}O_4N_3Cl$ requires C, 61·7; H, 4·4; N, 11·4%).

Stannous Chloride Reductions.—5-Amino-4-phenyl-2-*p*-nitrobenzylglyoxaline hydrochloride (15 g.) was added in small portions during 2 hours to a solution of hydrated stannous chloride (36 g.) in concentrated hydrochloric acid (90 c.c.) with stirring at 0—5°. A further 50 c.c. of the acid was then added, and stirring continued for 1 hour at 0°. After 12 hours at 0°, the mixture was evaporated to dryness *in vacuo* (at 60—70°), the residue dissolved in water (300 c.c.), and the tin precipitated with hydrogen sulphide. Filtration, and evaporation of the filtrate *in vacuo* at 60—70°, gave a crude solid (8 g.) which crystallised from methanol–ethyl acetate in colourless needles of *5-amino-4-phenyl-2-p-aminobenzylglyoxaline dihydrochloride* (7·6 g.), decomp. above 260° (Found : C, 56·8; H, 5·35; N, 16·3; Cl, 20·95. $C_{18}H_{18}N_4Cl_2$ requires C, 56·95; H, 5·35; N, 16·6; Cl, 21·05%). It was soluble in water and ethanol but insoluble in ether and ethyl acetate. It could be diazotised. Under similar reduction conditions, the analogous 2-*p*-nitrophenyl hydrochloride (10 g.) gave a crude product (8 g.) which crystallised from aqueous ethanol, giving colourless prisms of *5-amino-4-phenyl-2-p-aminophenylglyoxaline dihydrochloride dihydrate*, m. p. 258° (decomp.) (Found : N, 15·4. $C_{17}H_{16}N_4Cl_2,2H_2O$ requires N, 15·6%), and 5-amino-4-phenyl-2-*m*-nitrobenzylglyoxaline hydrochloride (15 g.) gave a crude product which, after charcoal treatment in methanol, crystallised from ethanol–ethyl acetate to give colourless micro-crystals of *5-amino-4-phenyl-2-m-aminobenzylglyoxaline dihydrochloride* (6·7 g.), m. p. 233° (Found : C, 56·95; H, 5·45; N, 16·3. $C_{18}H_{18}N_4Cl_2$ requires C, 56·95; H, 5·4; N, 16·65%). All were soluble in water, their bases being precipitated with alkali. They could all be diazotised.

Xanthines.—5-Amino-4-carbethoxy-2-*p*-nitrobenzylglyoxaline hydrochloride (52 g.), suspended in pyridine (200 c.c.) containing methyl *iso*cyanate (20 c.c.), was slowly heated, and finally refluxed for 1 hour. Two further portions (20 c.c. each) of methyl *iso*cyanate were added at hourly intervals to the mixture at 0°, and refluxing continued for 3 hours in all. About 70 c.c. of pyridine were removed *in vacuo* at 60—80°, methanol (500 c.c.) was added, and the crude solid (37·4 g.) crystallised from pyridine–methanol to give colourless needles of *5-methylureido-4-carbethoxy-2-p-nitrobenzylglyoxaline*, m. p. 242° (decomp.) (Found : C, 52·0; H, 5·05; N, 20·2. $C_{15}H_{17}O_5N_5$ requires C, 51·85; H, 4·95; N, 20·2%). The preceding ureido-compound (2 g.) was boiled for 1 minute in a mixture of 10% aqueous sodium hydroxide (15 c.c.) and water (45 c.c.). On acidification the crude purine was precipitated. Repeated precipitation with acid from its solution in dilute ammonia gave *8-p-nitrobenzyl-1-methylxanthine* (1·4 g.), m. p. >300° (decomp.), as a yellow solid (Found : C, 51·5; H, 4·0. $C_{13}H_{11}O_4N_5$ requires C, 51·8; H, 3·7%).

5-Methylureido-4-carbethoxy-2-*p*-nitrobenzylglyoxaline (4·5 g.) was reduced with stannous chloride and concentrated hydrochloric acid, as above. The crude reduction product (2·5 g.), m. p. 194° (decomp.), was boiled for 1 minute in 5% aqueous sodium hydroxide solution (100 c.c.), acidified with acetic acid, and the precipitate converted into the hydrochloride by boiling with 8% ethanolic hydrochloric acid (35 c.c.) and ethanol (20 c.c.). Crystallisation from water gave lustrous needles of *8-p-aminobenzyl-1-methylxanthine hydrochloride* (2 g.), m. p. 349—350° (decomp.) (Found : C, 51·3; H, 4·95; N, 22·8; Cl, 11·3. $C_{13}H_{14}O_2N_5Cl$ requires C, 50·7; H, 4·6; N, 22·8; Cl, 11·5%). It was very sparingly soluble in hot ethanol and cold water.

5-Amino-4-carbethoxy-2-benzylglyoxaline hydrochloride (3 g.), pyridine (10 c.c.), and phenyl *iso*cyanate (1·5 c.c.) were refluxed for 1 hour. Treatment with ethanol (10 c.c.) and water (20 c.c.) gave a crude solid (3 g.) which crystallised from methanol (20 c.c.) to give colourless hair-like needles of *5-phenylureido-4-carbethoxy-2-benzylglyoxaline*, m. p. 186—187° (Found : C, 65·9; H, 5·5; N, 15·4. $C_{20}H_{20}O_3N_4$ requires C, 66·1; H, 5·9; N, 15·1%). It was moderately soluble in methanol, ethanol, and ethyl acetate. The phenylureido-compound (1·77 g.) was converted with alkali, as above, into *1-phenyl-8-benzylxanthine* (0·68 g.), m. p. 316—318° (decomp.) (Found : N, 17·6. $C_{18}H_{14}O_2N_4$ requires N, 17·5%). It gave a positive murexide test.

Mannich Reaction.—5-Amino-4-carbethoxyglyoxaline (3·1 g.) (Cook, David, Heilbron, and Thomas, *loc. cit.*), trioxymethylene (0·66 g.), diethylamine (1·68 g.), and ethanol (15 c.c.) were refluxed for 2 hours and then concentrated *in vacuo*. The red gummy residue was dissolved in 7·8% ethanolic hydrochloric acid (30 c.c.), kept for 3 days at 0°, and the jelly-like product was poured into ether and filtered off. Crystallisation of the crude product (4·4 g.) from ethanolic hydrochloric acid gave colourless micro-crystals of *5-amino-4-carbethoxy-2-diethylaminomethylglyoxaline dihydrochloride*, m. p. 192—193° (Found : C, 42·0; H, 7·2; N, 17·8. $C_{11}H_{22}O_2N_4Cl_2$ requires C, 42·2; H, 7·1; N, 17·9%). The reaction can also be performed in ethanolic hydrochloric acid (2 mols. of HCl). The compound could be diazotised.

TABLE III.

5-Aminoglyoxaline hydrochlorides.

Substituents: 4.	2.	Yield, %.	Crystalline form[f] and solvent.	M. p.[g]	Formula.	Analyses.	Found, %.	Req., %.
Me	Ph[a]	76	Prisms; MeOH–Et_2O	264—265°[a]	$C_{10}H_{11}N_2Cl$	C	57·05	57·3
						H	5·65	5·75
						N	20·1	20·05
						Cl	17·1	16·95
CO_2Et	Ph[a]	82[a]	Microcrystals; EtOH	218—220[a]	—		—	
Ph	Ph[a]	95	Very pale lemon needles; MeOH	261[a]	$C_{15}H_{13}N_2Cl$	Cl	13·0	13·0
CO_2Et	*p*-$NO_2{\cdot}C_6H_4$[a]	98	Yellow silky needles; MeOH	277[a]	$C_{12}H_{12}O_4N_4Cl,1H_2O$	C	44·2	43·6
						H	4·8	4·6
						N	17·0	17·0
						Cl	11·0	10·75
						H_2O	5·7	5·4
Ph	*p*-$NO_2{\cdot}C_6H_4$[a]	67[a]	Orange-yellow microcrystals; EtOH–Et_2O	268—269[a]	$C_{15}H_{11}O_2N_4Cl$	C	56·5	56·85
						H	4·2	4·1
						N	17·3	17·7
Ph	*p*-C_6H_4Cl[a]	90	Yellow microcrystals; MeOH–Et_2O	Decomp. above 260°	$C_{15}H_{12}N_2Cl_2$	C	58·8	58·8
					$C_{15}H_{12}N_2Cl_2$	H	4·35	4·3
						N	13·8	13·7
						Cl	23·2	23·2
CO_2Et	3 : 4-$(OMe)_2C_6H_3$[b]	66	Needles; EtOH	233[a]	$C_{14}H_{16}O_4N_4Cl$	N	12·5	12·8
						Cl	10·5	10·8
Ph	3 : 4-$(OMe)_2C_6H_3$[a, b]	60—70	Pale lemon-yellow rods; MeOH	253—254[a]	$C_{17}H_{16}O_2N_4Cl$	N	12·5	12·7
						Cl	10·45	10·7
CO_2Et	CH_2Ph[b]	94[c]	Prismatic needles; MeOH–Et_2O	195—196[a]	$C_{13}H_{15}O_2N_4Cl$	N	14·8	14·9
Ph	CH_2Ph[a]	80[a]	EtOH	183—183·5[a]	$C_{16}H_{13}N_2Cl$	C	67·2	67·2
						H	5·6	5·65
						N	14·8	14·7
						Cl	12·5	12·4
CO_2Et	*p*-$NO_2{\cdot}C_6H_4{\cdot}CH_2$[a]	90	Microcrystals; EtOH–$CH_2{\cdot}CO_2Et$	226[a]	$C_{13}H_{14}O_4N_4Cl$	N	17·1	17·15
Ph	*p*-$NO_2{\cdot}C_6H_4{\cdot}CH_2$[a]	80[a]	Pale lemon needles; MeOH	232[a]	$C_{16}H_{13}O_2N_4Cl$	C	58·2	58·1
						H	4·65	4·6
						N	17·3	16·95
						Cl	11·0	10·7
Ph	*p*-$Cl{\cdot}C_6H_4{\cdot}CH_2$[a]	85	Microcrystals; EtOH–$CH_2{\cdot}CO_2Et$	225[a]	$C_{16}H_{12}N_2Cl_2$	C	59·7	60·0
						N	4·85	4·7
						N	12·9	13·1
						Cl	22·5	22·3
Ph	*p*-$OH{\cdot}C_6H_4{\cdot}CH_2$[a]	83	Needles; H_2O	255[a]	$C_{16}H_{14}ON_2Cl$	C	63·8	63·7
						H	5·35	5·35
						N	13·6	13·9
						Cl	11·95	11·8

Ph	*m*-$NO_2{\cdot}C_6H_4{\cdot}CH_2$ [b]	79 [e]	Pale yellow needles; EtOH	249 [a]	$C_{14}H_{13}O_3N_4Cl$	C	57·8	58·1
						H	4·85	4·6
						N	17·1	16·95
						Cl	10·7	10·7
Ph	*m*-$OH{\cdot}C_6H_4{\cdot}CH_2$ [b]	78 [e]	Cream prisms; EtOH	245 [a]	$C_{14}H_{14}ON_4Cl$	C	63·7	63·7
						H	5·65	5·35
						N	13·5	13·9
Ph	3 : 4-$(OMe)_2C_6H_3{\cdot}CH_2$ [b]	61 [d]	Prisms; EtOH	208—209	$C_{18}H_{20}O_3N_4Cl$	C	62·45	62·5
						H	5·55	5·85
						N	11·9	12·15
						Cl	9·9	10·25
CO_2Et	3 : 4-$(OMe)_2C_6H_3{\cdot}CH_2$ [b]	67	Prisms; MeOH–Et_2O	193—194 [a]	$C_{18}H_{20}O_3N_4Cl$	C	53·0	52·65
						H	6·2	5·9
						N	12·55	12·3
Ph	3 : 4-$(OCH_2O){:}C_6H_3{\cdot}CH_2$	24	Prisms; EtOH–Et_2O	141—143	$C_{17}H_{15}O_3N_4Cl$	N	12·9	12·75
						Cl	11·1	10·75
Ph	3 : 4 : 5-$(OMe)_3C_6H_2{\cdot}CH_2$ [c]	71	Needles; EtOH	218 [a]	$C_{19}H_{23}O_4N_4Cl$	C	60·85	60·7
						H	5·6	5·9
						N	11·0	11·2
						Cl	9·05	9·45
CO_2Et	α-$C_{10}H_7{\cdot}CH_2$ [b]	35	Prisms; EtOH–$CH_3{\cdot}CO_2Et$	203 [a]	$C_{17}H_{15}O_2N_4Cl$	C	61·85	61·5
						H	5·45	5·45
						N	12·7	12·7
						Cl	11·05	10·7
Ph	α-$C_{10}H_7{\cdot}CH_2$ [c]	82 [e]	Cream microcrystals; MeOH–$CH_3{\cdot}CO_2Et$	250 [a]	$C_{20}H_{15}N_4Cl$	C	71·7	71·5
						H	5·4	5·4
						N	12·4	12·5
						Cl	10·75	10·6
Ph	β-$C_{10}H_7{\cdot}CH_2$ [b]	81 [e]	Buff prisms; EtOH	246 [a]	$C_{20}H_{15}N_4Cl$	C	71·4	71·5
						H	5·6	5·4
						N	12·5	12·5
Ph	*n*-C_7H_{15} [b,h]	44 [e]	Needles; $CHCl_3$	123	$C_{18}H_{24}N_4Cl$	C	65·35	65·4
						H	8·25	8·25
						N	14·3	14·3
						Cl	12·1	12·1
CO_2Et	$-(CH_2)_6-$ Bis-compound [b]	44	Prisms; EtOH–$CH_3{\cdot}CO_2Et$	Efflorescence at at 120—132°, resolidifying, and m. p. 187°	$C_{28}H_{34}O_4N_4Cl_2,C_2H_5{\cdot}OH$	C	48·65	48·9
						H	7·1	7·45
						N	15·9	15·6
						Cl	13·3	13·2
						$C_2H_5{\cdot}OH$	8·1	8·5

[a] From the iminobenzyl thioether hydrochloride. [b] From the iminoethyl thioether hydrochloride. [c] 6—7 Hours' refluxing. [d] 10 Hours' refluxing. [e] 20 Hours' refluxing. [f] Colourless unless stated. [g] Cook, Davis, Heilbron, and Thomas, *loc. cit.* [h] Iminoethyl thioether hydrochloride not isolated; yield based on nitrile. [i] Robinson *et al.*, CPS, 549. [j] With decomposition.

Dry hydrogen chloride was passed into a solution of diethylaminoacetonitrile (15 g.), chloroform (250 c.c.), and ethanethiol (30 c.c.) at 0° for 2 hours. The hydrochloride of the nitrile was first precipitated and then further reacted, forming an upper oily layer. After being left for 2 days at 0°, the oily layer solidified, giving colourless prisms of diethylaminoacetimino ethyl thioether dihydrochloride (22 g.). It was very hygroscopic. The preceding thioiminoether dihydrochloride (10·5 g.), ethyl α-aminocyanoacetate (6·6 g.), and pyridine (4 g.) in chloroform (20 c.c.) were refluxed for 17 hours, then filtered from ammonium chloride (0·93 g.); the filtrate was evaporated to dryness *in vacuo*, and the black oily residue purified by crystallisation from 7·8% ethanolic hydrochloric acid (45 c.c.) to give the above glyoxaline (4 g.), m. p. and mixed m. p. 192—193°.

Aminoacetonitrile Condensations.—Aminoacetonitrile (1·75 g.) was added to a partial solution of *p*-nitrophenylacetimino benzyl thioether hydrochloride (10 g.) in chloroform (25 c.c.) containing pyridine (2·5 c.c.), shaken in an atmosphere of nitrogen for 7 hours, and left overnight at 0°; 8% ethanolic hydrochloric acid (20 c.c.) was added, and the crude solid (2·8 g.) filtered off. Crystallisation from methanol (120 c.c.) gave yellow needles of *5-amino-2-p-nitrophenylglyoxaline hydrochloride*, m. p. >250° (decomp.) (Found: N, 22·4; Cl, 13·7. $C_{10}H_{11}O_3N_4Cl$ requires N, 22·0; Cl, 13·9%). It was moderately soluble in water; after diazotisation it coupled with sodium β-naphthoxide to give a red dye. Similarly, β-naphthylacetimino ethyl thioether hydrochloride (9·4 g.) gave a crude solid (7·8 g.) which crystallised from methanol to give small colourless needles of *5-amino-2-β-naphthylmethylglyoxaline hydrochloride*, m. p. 154—155° (decomp.) (Found: C, 64·9; H, 5·45; Cl, 14·2. $C_{14}H_{14}N_3Cl$ requires C, 64·7; H, 5·45; Cl, 13·7%).

We thank the Directors of Beecham Research Laboratories Limited for permission to publish this paper, and Mr. L. J. Edwards for the determination of the absorption spectra.

BEECHAM RESEARCH LABORATORIES, LTD.,
BROCKHAM PARK, BETCHWORTH, SURREY.

[*Received, May 3rd*, 1950.]

---

535. *The Orientation of Disubstituted Fluoranthene Derivatives.*

By NEIL CAMPBELL, W. W. EASTON, (MISS) J. L. RAYMENT, and (in part) J. F. K. WILSHIRE.

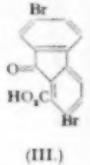
Bromination of fluoranthene gives **4**: 11-dibromofluoranthene, orientated by oxidation to **2**: 7-dibromofluorenone-1-carboxylic acid. By standard methods **4**: 11-dibromofluoranthene gives fluoranthene-**4**: 11-dicarboxylic acid which differs from the acid obtained by the interaction of oxalyl chloride and fluoranthene in the presence of aluminium chloride.

THE disubstitution products obtained from fluoranthene by bromination, etc., have not hitherto been rigidly orientated, though there is inconclusive evidence that such substances contain the substituents in the **4**: 11-positions (see Tobler *et al.*, *Helv. Chim. Acta*, 1941, **24**, 101E; Campbell *et al.*, *Nature*, 1950, **165**, 76). Von Braun's work shows clearly that one of the substituents must occupy the **4**-position (von Braun and Manz, *Annalen*, 1931, **488**, 111) and suggests that the second fills the 11- or 12-position. A decision in favour of the former comes from Waters (*J.*, 1948, 727) who points out that in polycyclic aromatic hydrocarbons substitution occurs at the same positions as those which are converted into carbonyl groups when the hydrocarbons are oxidised to quinones. In the present instance, as noted by Tobler *et al.* (*loc. cit.*), a **4**: 11-quinone (I) can be formulated while a **4**: 12-quinone cannot. Disubstitution of fluoranthene may, therefore, be expected to occur at positions **4** and **11**. The correctness of this prediction has now been shown by the proof that dibromination of fluoranthene gives **4**: 11-dibromofluoranthene (II).

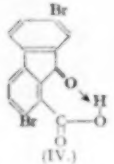
Chromic acid oxidation of dibromofluoranthene gave a dibromofluorenone-1-carboxylic acid, decarboxylation of which with quinoline and copper was accompanied by debromination to 2-bromofluorenone, thus strongly indicating that the original acid was **2**: 7-dibromofluorenone-1-carboxylic acid. That it is the bromine atom contiguous to the carboxyl group which is

(I.)

(II.)



(III.)



(IV.)

removed was shown by the stability of 2-bromo- and **2**: 7-dibromofluorenone to boiling quinoline and copper, and the decarboxylation under similar conditions of 2-bromofluorenone-1-carboxylic

acid and 7-bromofluorenone-1-carboxylic acid to fluorenone and 2-bromofluorenone respectively. Conclusive evidence was finally obtained by decarboxylation of the dibromo-acid with mercuric oxide at 180° (cf. Dziewonski and Khal, *Chem. Abstr.*, 1935, **19**, 2941) to yield 2 : 7-dibromofluorenone. The acid is therefore 2 : 7-dibromofluorenone-1-carboxylic acid (III) and the original substance must in consequence be 4 : 11-dibromofluoranthene (II).

In some of the oxidation experiments a monobromo-acid was isolated and it is probably 6-bromofluorenone-1-carboxylic acid, ring A having been disrupted. The possibility that ring C had been oxidised giving 4-bromonaphthalic acid was excluded since our acid is yellow, easily esterified, and does not react with *o*-phenylenediamine, whereas 4-bromonaphthalic acid is white, is not esterified even by diazomethane, and readily forms two benziminazole derivatives with *o*-phenylenediamine.

Dehalogenation of aromatic compounds containing a carboxyl group adjacent to the halogen atom has frequently been observed, *o*-halogenobenzoic acids and 8-bromo-1-naphthoic acid, for example, yielding the halogen-free acids when boiled with toluene and copper bronze (Rule *et al.*, *J.*, 1934, 168; Pursell, Thesis, Edinburgh). Rather unexpectedly, similar treatment failed to debrominate 2 : 7-dibromofluorenone-1-carboxylic acid. Rule (*loc. cit.*) showed that such dehalogenations are effected by reduction, the requisite hydrogen coming from the carboxyl group. Presumably in our acid there is some form of interaction between the carboxyl and carbonyl groups as shown in (IV). This formula is very similar to the oxonium formula for fluorenone-1-carboxylic acid advanced by Hantzsch (*Ber.*, 1916, **49**, 226), who, however, applied his formula only to the solid acid and regarded the acid in neutral solvents such as ethanol as having the norm " ketoid " form.

4 : 11-Dibromofluoranthene is a useful reference substance. For example, it is converted into 4 : 11-dicyanofluoranthene, hydrolysis of which gives fluoranthene-4 : 11-dicarboxylic acid which was at first regarded as identical with the acid obtained by Campbell and Easton (*J.*, 1949, 340) by the action of oxalyl chloride on fluoranthene in the presence of aluminium chloride. Recent investigations on larger quantities of material (Campbell and Wilshire, unpublished results) show, however, that the two acids are different. It would seem, therefore, that the Friedel–Crafts reaction, unlike bromination, does not give 4 : 11-disubstituted products.

Attempts to hydrolyse the above dicyano-compound by conversion into the imino-ethers (Hager *et al.*, *J. Amer. Chem. Soc.*, 1944, **66**, 1982) failed. The stability of the 4-cyano-group is not surprising since we found that α-naphthonitrile, in contrast to the β-compound, is not hydrolysed by this method, but the failure of the 11-cyano-group to react was unexpected.

The bromine atoms in 4 : 11-dibromofluoranthene are inert to magnesium, but are removed by nickel–aluminium alloy and alkali.

Experimental.

All chromatographic adsorptions were carried out on alumina (Brockmann). Analyses were done by Drs. Weiler and Strauss (Oxford). Compounds marked with an asterisk have been mentioned in patent literature but without analytical data.

Oxidation of 4 : 11-*Dibromofluoranthene.*—Dibromofluoranthene was prepared by the bromination of fluoranthene by the method of Tobler *et al.* (*loc. cit.*). Chromic anhydride (AnalaR; 10 g.) in water (20 ml.) and glacial acetic acid (24 ml.) was added slowly to dibromofluoranthene (6 g.) in glacial acetic acid (400 ml.) just below the boiling point and the mixture refluxed for 3 hours. Chromic anhydride (14 g.) in water (20 ml.) and glacial acetic acid (100 ml.) was added and the mixture boiled for 3 hours. The solution was reduced to 100 ml. and poured into water (*ca.* 200 ml.). The precipitate was extracted with barium carbonate or potassium carbonate solution, acidification of which then yielded 2 : 7-*dibromofluorenone*-1-*carboxylic acid* (2 g., 32%), which separated from benzene and methanol as yellow needles, subliming at 200°, m. p. 269—272° (Found : C, 44·9; H, 1·9; Br, 40·9. $C_{14}H_6O_3Br_2$ requires C, 44·0; H, 1·6; Br, 41·9%). The acid when boiled with methanol and sulphuric acid gave no ester, but with diazomethane yielded the *methyl* ester, which crystallised from methanol in yellow prisms, m. p. 197° (Found : C, 45·6; H, 2·2; Br, 40·6. $C_{15}H_8O_3Br_2$ requires C, 45·5; H, 2·0; Br, 40·4%).

In some experiments the crude acidic product was boiled with an aqueous suspension of barium carbonate, and the boiling mixture filtered. Acidification of the residual barium carbonate gave 2 : 7-dibromofluorenone-1-carboxylic acid, m. p. 266—267°, showing no m. p. depression when mixed with a sample prepared as above. The filtrate on acidification with dilute hydrochloric acid gave 6(?)-*bromofluorenone*-1-*carboxylic acid*, which after crystallisation from glacial acetic acid and sublimation separated as yellow needles, m. p. 253—255° (Found : Br, 26·3. $C_{14}H_7O_3Br$ requires Br, 26·4%). The *methyl* ester, made by use of methanol and sulphuric acid, crystallised from methanol in pale yellow needles, m. p. 126—127° (Found : C, 57·2; H, 3·3; Br, 25·8. $C_{15}H_9O_3Br$ requires C, 56·8; H, 2·9; Br, 25·2%).

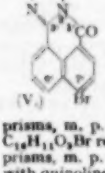
Decarboxylation of 2 : 7-*Dibromofluorenone*-1-*carboxylic Acid.*—The acid (0·5 g.) was heated at 180° with quinoline (15 ml.) and copper bronze for 30 minutes. The precipitate obtained by the addition of

dilute hydrochloric acid was dissolved in benzene and chromatographed on a column 3½″ × ½″. Development with benzene yielded a yellow zone which on extraction with ethanol gave 2-bromofluorenone, m. p. 141—142°, not depressed when mixed with an authentic sample.

The acid (0·5 g.), freshly precipitated mercuric oxide (0·32 g.), and water (5 ml.) were heated in a sealed tube at 185° for 30 hours, and the product refluxed with concentrated hydrochloric acid (15 ml.) for 3 hours. The residue was extracted first with ether, then benzene, and the combined extracts were washed with 5% aqueous potassium carbonate and dried (Na_2SO_4). Evaporation gave a solid which was dissolved in benzene and chromatographed on a column 4″ × ½″. Development with benzene gave a yellow band which on elution and evaporation gave 2 : 7-dibromofluorenone, m. p. 201—202°, not depressed when mixed with an authentic sample prepared by the oxidation of 2 : 7-dibromofluorene with chromic anhydride (AnalaR) and acetic acid. The potassium carbonate solution on acidification yielded some of the original acid.

Oxidation of **4**-*Bromofluoranthene.*—4-Bromofluoranthene (2·5 g.) was oxidised by chromic anhydride (AnalaR) as described above and the resulting 2-bromofluorenone-1-carboxylic acid when crystallised from glacial acetic acid was obtained as yellow needles, m. p. 252—254° (von Braun *et al.*, *Annalen*, 1932, **496**, 107, give 252°) (0·8 g., 30%) (Found : C, 55·1; H, 2·3; Br, 26·5. Calc. for $C_{14}H_7O_3Br$: C, 55·4; H, 2·3; Br, 26·4%). The acid could not be esterified by methanol and sulphuric acid, but with diazomethane yielded the *methyl* ester, yellow needles (from methanol), m. p. 140—142° (Found : C, 56·5; H, 3·1. $C_{15}H_9O_3Br$ requires C, 56·8; H, 2·8%). Decarboxylation with quinoline and copper at 180° gave a product which after chromatographic purification separated as a yellow oil, identified as fluorenone by its 2 : 4-dinitrophenylhydrazone, m. p. 295—297°, not depressed on admixture with an authentic sample (Found : N, 15·2. Calc. for $C_{19}H_{10}O_4N_4$: N, 15·6%).

Preparation and Properties of **4**-*Bromonaphthalic Acid.*—4-Bromoacenaphthene (4 g.) in glacial acetic acid (60 ml.) was heated with sodium dichromate (20 g.) for 1 hour on the water-bath and filtered. The filtrate with water (200 ml.) gave a precipitate which was dissolved in ether and extracted with 2·5% aqueous potassium carbonate, acidification of which then gave 4-bromonaphthalic acid. Crystallisation from benzene yielded needles, m. p. 218—219° (lit., 220°). Unsuccessful attempts were made to esterify the acid with methanol and sulphuric acid or with diazomethane. Equimolecular quantities of the acid and *o*-phenylenediamine were boiled for a few minutes in glacial acetic acid and gave on cooling a palpable mixture, subliming at *ca.* 165°, m. p. 225—266°, which was separated into its components by boiling benzene. The less soluble 7′(6′?)-*bromo*-1′-*keto*-2′-*azaperinaphthano*(2′ : 3′-1 : 2)*benziminazole* (V) was purified by repeated crystallisations from toluene which gave yellow needles, m. p. 270—272° after subliming at 228° (Found : N, 8·1. $C_{18}H_9N_3OBr$ requires N, 8·0%). The more soluble *isomer* crystallised from benzene in yellow needles, m. p. 219—221° (Found : N, 8·3; Br, 21·8. $C_{18}H_9N_3OBr$ requires N, 8·0; Br, 22·9%).



(V.)

7-Bromofluorenone-1-*carboxylic Acid.*—Fluorenone-1-carboxylic acid (2 g.) was added to bromine (25 ml.). The mixture at first gave a thick paste, but when kept overnight became liquid again and pouring it into water gave *7-bromofluorenone*-1-*carboxylic acid* which was washed with ethanol, then crystallised first from glacial acetic acid and then from benzene in red elongated prisms, m. p. 226—228° (1·6 g., 60%) (Found : C, 55·3; H, 2·8; Br, 27·6. $C_{14}H_7O_3Br$ requires C, 55·4; H, 2·3; Br, 26·4%). The acid readily yielded the *ethyl* ester with ethanol and sulphuric acid; this formed yellow prisms, m. p. 102—103°, from ethanol or benzene–light petroleum (b. p. 40—60°) (Found : Br, 23·8. $C_{16}H_{11}O_3Br$ requires Br, 24·1%). The *methyl* ester, similarly obtained, separated from benzene in yellow prisms, m. p. 164° (Found : Br, 25·4. $C_{15}H_9O_3Br$ requires Br, 25·2%). Decarboxylation of the acid with quinoline and copper at 180° for 45 minutes gave 2-bromofluorenone, m. p. 136° either alone or when mixed with an authentic sample.

4 : 11-*Dicyanofluoranthene.*—**4** : 11-Dibromofluoranthene (1 mol.) and cuprous cyanide (2·2 mols.) were thoroughly mixed and heated for 6 hours at 260° (cf. B.P. 533,962). The product was extracted successively with chloroform, xylene, and chlorobenzene, which yielded dibromofluoranthene, fluoranthene, and **4** : 11-*dicyanofluoranthene* • respectively. The last sublimed in yellow crystals at *ca.* 200° and had m. p. 321—323° (Found : N, 10·3. $C_{18}H_8N_2$ requires N, 11·1%). Oxidation of the dicyano-compound gave a *substance*, soluble in alkali, which contained only a trace of nitrogen (Found : C, 50·8; H, 3·2; N, 0·4%). Hydrolysis of the cyano-groups had, therefore, occurred and the analysis shows that the resulting acid cannot be the expected fluorenonetricarboxylic acid ($C_{19}H_8O_7$ requires C, 61·5; H, 2·65%). An attempt to esterify the acid by boiling it for 24 hours with methanol and sulphuric acid was unsuccessful.

4 : 11-Dicyanofluoranthene (0·1 g.) was boiled for 1 hour with glacial acetic acid (2 ml.), concentrated sulphuric acid (1 ml.), and water (1 ml.). The resulting **4** : 11-*fluoranthenedicarboxylic acid* • was only slightly soluble in the common organic solvents, but sublimed at *ca.* 280° to give yellow needles, m. p. >360° (Found : C, 75·2; H, 4·2. $C_{18}H_{10}O_4$ requires C, 74·5; H, 4·2%). The acid (0·35 g.) was boiled overnight with methanol (2 ml.) and concentrated sulphuric acid (8 drops), and the resulting flocculent precipitate dissolved in benzene, passed through a chromatographic column 4″ × ½″, and developed with benzene. From the eluate *dimethyl fluoranthene*-**4** : 11-*dicarboxylate* was obtained as a pale yellow flocculent mass (from methanol–glacial acetic acid), m. p. 168—169°, subliming at 145° (Found : C, 75·3; H, 4·8. $C_{20}H_{14}O_4$ requires C, 75·5; H, 4·4%). It gave a m. p. depression of 30° when mixed with the dimethyl ester of the diacid obtained from fluoranthene and oxalyl chloride (Campbell and Easton, *loc. cit.*).

Debromination of **4** : 11-*Dibromofluoranthene.*—Raney nickel–aluminium alloy (3·5 g.) was added to a boiling solution of **4** : 11-dibromofluoranthene (0·3 g.) in ethanol (10 ml.) and 10% ethanolic potassium hydroxide (75 ml.). The alloy was added in four portions during 10 minutes. The mixture was heated until all the alloy had reacted (1—1½ hours). The hot solution was filtered, and water was added to the

filtrate which was then made acid to Congo-red paper by concentrated hydrochloric acid. The precipitate on crystallisation proved to be fluoranthene, m. p. and mixed m. p. 110° (0·1 g., 60%).

The authors thank the Department of Scientific and Industrial Research for a maintenance grant to one of them (J. L. R.) and the Anglo-Iranian Oil Co. Ltd. for a grant.

THE UNIVERSITY, EDINBURGH. [*Received, January 17th*, 1950.]

---

536. *Organic Fluorides. Part IV. Fluorination of Hydroaromatic Hydrocarbons by Use of a Gold Catalyst.*

By R. N. HASZELDINE and F. SMITH.

Vapour-phase fluorination using a gold catalyst gives better yields of fluorocarbons from hydroaromatic hydrocarbons than from the parent aromatic hydrocarbons. Ethylcyclohexane was found to be the best hydrocarbon for the preparation of a C_8F_{18} fluorocarbon.

IN Part III (*J.*, 1950, 2689) the optimum conditions for the fluorination of aromatic hydrocarbons were determined. From the point of view of fluorine economy, it is apparent that since hydroaromatic hydrocarbons will consume more fluorine than unsaturated or aromatic hydrocarbons during complete fluorination, it would be advantageous to use the unsaturated compounds. The experiments recorded herein prove, however, that higher yields of fluorocarbons are obtained from hydroaromatic than from aromatic hydrocarbons (Table I). Hence,

TABLE I.

The effect of unsaturation upon the yield of fluorocarbon.

Hydrocarbon.	Fluorocarbon.	Yield, %.
Ethylbenzene	Perfluoroethylcyclohexane	9·6
Ethylcyclohexane	"	21
Mesitylene	Perfluoro-1 : 3 : 5-trimethylcyclohexane	5·9
1 : 3 : 5-Trimethylcyclohexane	"	11·2
m-Xylene	Perfluoro-1 : 3-dimethylcyclohexane	4·5
1 : 3-Dimethylcyclohexane	"	15·4
Tetrahydronaphthalene	Perfluorodecahydronaphthalene	11·4
Decahydronaphthalene	"	18·8

as far as fluorination is concerned, the double bond in aromatic as well as in aliphatic hydrocarbons is a position of weakness (cf. Part I, *J.*, 1949, 3021). The results also show that, under the conditions employed in this work, fluorination of hydroaromatic hydrocarbons is attended by less decomposition and less polymerisation than is the case with aromatic hydrocarbons. These results should be compared with those of Cady *et al.* (*Ind. Eng. Chem.*, 1947, **39**, 290), published since this work was completed, which indicated that aromatic hydrocarbons give higher yields of fluorocarbons than the paraffinic hydrocarbons when fluorinated in the vapour phase in the presence of silver-plated copper turnings.

The rôle played by the gold-plated copper turnings in vapour-phase fluorination is not immediately apparent. Before the recent fluorination studies (see Parts I, II, and III of this series; Cady *et al.*, *loc. cit.*), it was recorded by Fredenhagen and Cadenbach (*Ber.*, 1934, **67**, 928) that the presence of copper, iron, silver, or cerium filling agents gave improved yields during fluorination. This improvement was ascribed to the dispersion of the reactants and no catalytic effect was suspected. Bigelow and his co-workers then confirmed and extended the beneficial effect of copper gauze during fluorination. The view has been advanced that the reaction is the vapour phase involves free radicals (Bigelow *et al.*, *J. Amer. Chem. Soc.*, 1937, **59**, 198; 1938, **60**, 427; 1939, **61**, 3552; 1940, **62**, 267, 1171, 3302; 1941, **63**, 788, 2792; *Ind. Eng. Chem.*, 1947, **39**, 360; Miller, *J. Amer. Chem. Soc.*, 1940, **62**, 341), and that it is a catalytic one (Cady *et al.*, *loc. cit.*; Part I, *loc. cit.*). Moreover, the elements which aid fluorination, such as gold, silver, copper, cobalt, etc., show variable valency, and the higher fluorides of some of these metals are themselves capable of acting as fluorinating agents (McBee and Bechtol, *Ind. Eng. Chem.*, 1947, **39**, 380; Fowler *et al.*, *ibid.*, pp. 292, 343). This would, therefore, lead to the suggestion that, in part, the rôle of the catalyst is that of a halogen carrier and that its action is due to the formation of the higher fluoride, which in contact with hydrocarbon vapour effects the introduction of fluorine into the molecule. Examination of the gold catalyst after several experiments, however, has repeatedly shown that the metal surface is only slightly

attacked and little increase in weight takes place. Since auric fluoride is readily detectable by its orange colour (Moissan, *Compt. rend.*, 1889, **109**, 807), it seems that there is not the complete conversion which might be expected if the gold (as a fluoride) is acting solely as a halogen carrier. Whatever the exact rôle of the gold may be, it is certainly an important one, for in time it is slowly attacked and the auric and copper fluorides are gradually carried to the base of the reaction vessel by the gas streams, a development accompanied by diminishing yields of fluorocarbon.

At the time (1940—1946) when this and the preliminary work (Parts I and II) was being carried out, it seemed that, although a vast improvement had been brought about by the use of gold and silver as catalysts, vapour-phase procedures involving the direct use of elementary fluorine were unlikely to become generally useful or economical on a large scale. Since that time no experimental evidence has been produced which would justify any alteration of this view. In a forthcoming communication, however, it will be shown that the indirect use of fluorine for the fluorination of hydrocarbons by cobalt trifluoride affords better yields of fluorocarbons (see also Fowler *et. al.*, *loc. cit.*).

Experimental.

Apparatus and Procedure.—The apparatus used for this work has been fully described in Part III (*loc. cit.*). The catalyst was replaced when its activity (tested against benzene or heptane as described in Parts I and III) was seen to be reduced. The procedure adopted was the same as that for the work in Part III.

(A) *Fluorination of* 1 : 3-*Dimethylcyclohexane.*—This was best accomplished by treating the hydrocarbon (17 g.) at the rate of 2 c.c./hr. (reservoir temp. 75°) with fluorine (13 g./hr.) at 200°. The hydrocarbon was diluted with 19 l. of nitrogen/hr. and the fluorine with 18 l. of nitrogen/hr. The yield of crude fluorocarbon (22 g.) corresponded to a recovery of 129%. Fractional distillation gave: fraction 1, (decomposition products), 6·3 g., b. p. 40—95°; fraction 2 (perfluorodimethylcyclohexane), 9·9 g., b. p. 95—105°; fraction 3 (hydrofluorocarbon), 4·7 g., b. p. 105—170°. No polymer was obtained in this experiment but it was produced when a high rate of addition of hydrocarbon and a high nitrogen dilution of the reactants were employed. The yield of fluorocarbon formed from the saturated hydrocarbon was much greater than that produced from the parent aromatic hydrocarbon (see Part III). This observation, hitherto unknown, was substantiated by the experiments recorded below. Purification of 28·1 g. of the crude fluorocarbon (fraction 2) obtained in this way gave perfluoro-1 : 3-dimethylcyclohexane (24·2 g.), b. p. 101·5°, D_4^{25} 1·828 g./c.c., n_D^{25} 1·283, γ^{25} 15·1 dynes/cm., η^{25} 19·3 millipoises.

(B) *Fluorination of Ethylcyclohexane.*—This proved to be the best hydrocarbon for producing C_8F_{16} by the vapour-phase catalytic procedure. Treatment of ethylcyclohexane (24 g.) [added at the rate of 2·7 c.c./hr.) (reservoir temp. 105°) and diluted with 10 l. of nitrogen/hr.] with fluorine (15 g./hr. diluted with 10 l. of nitrogen/hr.) gave 78·1 g. of crude product, 29·2 g. of which collected in traps *A* and *B* and 48·9 g. in the U-tubes. Distillation of the U-tube condensate gave: fraction 1, 9·3 g. (decomposition products) b. p. 20—95°; fraction 2, crude perfluoroethylcyclohexane, 27·4 g., b. p. 95—105°; fraction 3, hydrofluorocarbon, 10·4 g., b. p. 105—170°. The distillation residue of polymeric material was 0·5 g., b. p. >170°. The "recovery" was approximately 200%. Purification of a total of 161 g. of fraction 2 obtained in this way afforded perfluoroethylcyclohexane (121 g.; yield 75—80% of ethylcyclohexane), b. p. 101·5°, f. p. −60°, D_4^{25} 1·826, n_D^{25} 1·283. After a number of experiments the polymeric material which collected in traps *A* and *B* was fractionated to give stable colourless fluoro-oils of the same type as those isolated previously in much greater quantity from ethylbenzene.

(C) *Fluorination of* 1 : 3 : 5-*Trimethylcyclohexane.*—A typical experiment was carried out at 200° by treating the hydrocarbon (14 g.) (3·5 c.c./hr.) (reservoir temp. 125°) diluted with 16 l. of nitrogen/hr. with fluorine (15 g./hr. diluted with 14 l. of nitrogen/hr.). This procedure afforded 7·2 g. in traps *A* and *B* and 16·3 g. in the U-tubes. The latter gave: fraction 1, decomposition products, 3·7 g., b. p. 40—120°; fraction 2, crude C_9F_{18}, 7·9 g., b. p. 120—128°; fraction 3, hydrofluorocarbon, 2·6 g., b. p. 128—170°; fraction 4, polymeric material, 0·7 g., b. p. >170°. These figures correspond to a recovery of 106%. Refractionation of polymeric material corresponding to fraction 4 gave oils of the usual type, and from the reactor a small amount of a wax-like polymer was recovered.

Table II shows a detailed analysis of these results and those on the fluorination of mesitylene. The advantage of using the hydroaromatic hydrocarbon for fluorination instead of the corresponding aromatic hydrocarbon is quite apparent though the difference is not as marked as with ethylbenzene and ethylcyclohexane. Purification of fraction 2 in the usual way yielded perfluoro-1 : 3 : 5-trimethylcyclohexane, b. p. 124·6°, D_4^{25} 1·89, n_D^{25} 1·294.

Table II.

Material fluorinated.	$\frac{\text{Wt. } C_9F_{18}}{\text{Wt. hydrocarbon}} \times 100$.	C_9F_{18} in total distillate (%).	Decomposition products (b. p. 40—124°) in crude yield (%).	Hydrofluorocarbon (b. p. 125—170°) in crude yield (%).
Trimethylcyclohexane	26	26	36	24
Mesitylene *	10	11	52	26

* Results from Part III (*loc. cit.*).

(D) *Fluorination of Tetrahydronaphthalene.*—Under the best conditions for the fluorination (temp. 380°; hydrocarbon 3 c.c./hr. diluted with 15 l. of nitrogen/hr.; temp. of reservoir 185°; fluorine 14 g./hr. diluted with 10 l. of nitrogen/hr.), 20 g. of tetrahydronaphthalene gave 24·4 g. of crude fluorocarbon which upon distillation yielded: fraction 1, decomposition products, 7·0 g., b. p. 40—135°; fraction 2, crude perfluorodecahydronaphthalene, 9·2 g., b. p. 135—146°; fraction 3, hydrofluorocarbon, 5·9 g., b. p. 146—210°. It was noted as in previous fluorinations that increasing the nitrogen dilution of the hydrocarbon produced more hydrofluorocarbon and polymeric material.

Purification of the crude fluorocarbon corresponding to fraction 2 (31·4 g.) yielded perfluorodecahydronaphthalene (10·2 g.), b. p. 142°, f. p. −15°, D_4^{20} 1·919, n_D^{20} 1·309, γ^{20} 18·4, χ^{20} 51·1 (Found: C, 25·4; F, 73·7%; *M*, 454: Calc. for $C_{10}F_{18}$: C, 26·0; F, 74·0%; *M*, 462). McBee and Bechtol (*loc. cit.*) give b. p. 140°, f. p. −7° to −10°, D_4^{20} 1·9456, n_D^{20} 1·3118 for this compound (cf. Musgrave and Smith, *J.*, 1949, 3021).

The series of experiments carried out with this compound showed that much more decomposition occurred with tetrahydronaphthalene than with either benzene or toluene. Some polymerisation also occurred, and the product collected in trap *A* afforded the usual fractions of colourless fluoro-oils (b. p. 150—240°/10 mm.) and a glassy solid, b. p. 240—300°/10 mm.

(E) *Fluorination of Decahydronaphthalene.*—In one *set* a series of experiments fluorine (14 g./hr.) diluted with 10 l. of nitrogen/hr. was allowed to react with decahydronaphthalene (2 g./hr.) diluted with 10 l. of nitrogen/hr. at 370° during 12 hours. The crude fluorocarbon (32·8 g.) collected in the U-tubes was washed with water, dried (phosphoric oxide) and distilled to give: fraction 1, decomposition products, 5·3 g., b. p. 40—135°; fraction 2, crude perfluorocarbon, 15·1 g., b. p. 135—146°; fraction 3, hydrofluorocarbon, 6·7 g., b. p. 146—210°; fraction 4, polymer, 0·15 g., b. p. >210°. The crude perfluorodecahydronaphthalene formed 63% of the weight of the starting product; this should be compared with the best figure of 46% produced during the fluorination of tetrahydronaphthalene. When purified in the manner described in Part III, the perfluorodecahydronaphthalene had the same properties as those described in Section D (Found: F, 73·6. Calc. for $C_{10}F_{18}$: F, 74·0%).

The authors thank (the late) Sir Norman Haworth, F.R.S., and Professor M. Stacey, F.R.S., for their interest in this work. They also thank the Director-General of Scientific Research for permission to publish it.

THE CHEMISTRY DEPARTMENT,
THE UNIVERSITY, EDGBASTON, BIRMINGHAM, 15. [*Received, February 16th*, 1950.]

---

537. *The Reactions of Fluorocarbon Radicals. Part III. The Synthesis of Heptafluorobutyric Acid.*

By R. N. HASZELDINE.

The interaction of heptafluoroiodopropane and acetylene yields 3 : 3 : 4 : 4 : 5 : 5 : 5-heptafluoro-1-iodopent-1-ene, which, on treatment with permanganate, gives heptafluorobutyric acid. Salts and derivatives of the acid are described, and the synthesis of long-chain fluoro- and fluorohalogeno-acids is discussed.

IN Part I (Haszeldine, *J.*, 1949, 2856), the interaction of trifluoroiodomethane and tetrafluoroethylene was shown to yield compounds of general formula $CF_3{\cdot}[CF_2{\cdot}CF_2]_n{\cdot}I$, and several members of this series were briefly described. The isolation and reactions of individual members of this polymer series will be described in a later communication. The present communication describes the conversion of the compound where $n = 1$ (*i.e.*, C_3F_7I) into heptafluorobutyric acid, and illustrates the use of trifluoroiodomethane in synthetic organic fluorine chemistry.

The carbon–iodine bond in heptafluoroiodopropane splits homolytically when the compound is irradiated with ultra-violet light or heated, in a manner analogous to that shown for trifluoroiodomethane and pentafluoroiodoethane (Haszeldine and Emeléus, *Research*, 1948, **1**, 715). Under these conditions an addition-polymerisation reaction occurs with acetylene (cf. Haszeldine, *Nature*, 1950, **165**, 152) to give mainly the first member of the series $CF_3{\cdot}CF_2{\cdot}CF_2{\cdot}[CH{:}CH]_n{\cdot}I$:

$$C_3F_7I \longrightarrow C_3F_7{\cdot} + {\cdot}I$$
$$C_3F_7{\cdot} + CH{:}CH \longrightarrow C_3F_7CH{:}CH{\cdot}$$
$$C_3F_7CH{:}CH{\cdot} + C_3F_7I \longrightarrow C_3F_7CH{:}CHI + C_3F_7{\cdot}$$

It has been shown (Part II, Haszeldine, *J.*, in press; *Nature*, 1950, **166**, 192) that the double bond adjacent to a perfluoroalkyl group such as CF_3 or C_3F_7 is susceptible to permanganate oxidation; similarly, treatment of the heptafluoroiodobutene with alkaline potassium permanganate gives heptafluorobutyric acid in good yield. The latter resembles trifluoroacetic acid, since it is a strong acid (approaching a mineral acid) and has a low boiling point (121°) compared with

the corresponding unhalogenated acid (163·5°); it has an odour similar to that of pentafluoropropionic acid (Haszeldine and Leedham, unpublished observations).

Heptafluorobutyric acid shows many of the reactions of a carboxylic acid, and has been characterised by the formation of the following crystalline salts of organic bases : piperazinium bisheptafluorobutyrate, nitron heptafluorobutyrate, and benzylamine heptafluorobutyrate. The acid forms well-defined metallic salts of which the sodium, potassium, mercuric, and silver compounds have been obtained pure. Silver heptafluorobutyrate is soluble in ether and benzene, as is silver perchlorate and silver trifluoroacetate (Swarts, *Bull. Soc. chim. Belg.*, 1939, **48**, 176). The mercuric salt, which is very soluble in water, gives a basic salt when heated in aqueous solution.

Ethyl heptafluorobutyrate was prepared in high yield by the standard procedure, and with ammonia gave the amide. Interaction of the amide and phosphoric oxide afforded the nitrile which is readily hydrolysed by aqueous alkali and which has a boiling point (1°) almost 120° below that of butyronitrile (b. p. 118°) (cf. $CF_3{\cdot}CN$, b. p. −64°, and $CH_3{\cdot}CN$, b. p. 82°).

Tetradecafluorobutyric anhydride and heptafluorobutyryl chloride were prepared in almost quantitative yield. The anhydride acetylated a phenol (β-naphthol) in the normal manner, although the product was readily hydrolysed. The acid chloride gave amides in the normal manner, the amide, anilide, and benzylamide being prepared. The characterisation of the perfluoro-carboxylic acids by the melting points of the amides must be carried out with care since the melting points of pentafluoropropionamide (95—96°) and heptafluorobutyramide (102—103°) are rather close, although appreciably different from that of trifluoroacetamide (75°).

Kauck and Diesslin (Abstracts, American Chemical Society 116th Meeting, Atlantic City, September, 1949, 9K) have described the synthesis of heptafluorobutyric acid by the electrochemical fluorination of butyric acid in liquid hydrogen fluoride, followed by hydrolysis of the acid fluoride so formed. Reid and Smith (*ibid.*, 9K) and Husted and Ahlbrecht (*ibid.*, 10K) give 119° as the boiling point of the fluoro-acid and state that the anhydride, acyl halide, salts, esters, amide, and anilide have been prepared.

Thus, two general methods appear to be available for the preparation of long-chain perfluoro-acids. The first by the electrochemical fluorination of the corresponding halogen-free acid, and the second by the use of members of the polymer series $CF_3{\cdot}[CF_2]_n{\cdot}I$, derived from trifluoroiodo-

$$\left.\begin{array}{l} CF_3I + C_2F_4 \longrightarrow CF_3{\cdot}[CF_2{\cdot}CF_2]_n{\cdot}I \\ C_2F_5I + C_2F_4 \longrightarrow C_2F_5{\cdot}[CF_2{\cdot}CF_2]_n{\cdot}I \end{array}\right\} CF_3{\cdot}[CF_2]_n{\cdot}I$$

methane and pentafluoroiodoethane and tetrafluoroethylene by application of the procedure described in the present communication :

$$CF_3{\cdot}[CF_2]_n{\cdot}I \xrightarrow{C_2H_2} CF_3{\cdot}[CF_2]_n{\cdot}CH{:}CHI \xrightarrow{KMnO_4} CF_3{\cdot}[CF_2]_n{\cdot}CO_2H$$

An alternative route lies through the reaction of the fluoro-iodides with ethylene, followed by dehydroiodination and oxidation (unpublished results) :

$$CF_3{\cdot}[CF_2]_n{\cdot}I \xrightarrow{C_2H_4} CF_3{\cdot}[CF_2]_n{\cdot}CH_2{\cdot}CH_2I \longrightarrow CF_3{\cdot}[CF_2]_n{\cdot}CH{:}CH_2 \xrightarrow{KMnO_4} CF_3{\cdot}[CF_2]_n{\cdot}CO_2H$$

Yet another method utilises the fact that trifluoroiodomethane and similar fluoro-iodides can be converted into the Grignard reagents which, on carboxylation, yield the expected acid (unpublished observations) :

$$CF_3{\cdot}[CF_2]_n{\cdot}I \xrightarrow{Mg} CF_3{\cdot}[CF_2]_n{\cdot}MgI \xrightarrow{CO_2} CF_3{\cdot}[CF_2]_n{\cdot}CO_2H$$

The interaction of trifluoroiodomethane, pentafluoroiodoethane, or of the fluoro-iodides $CF_3{\cdot}[CF_2]_n{\cdot}I$ with other fluoro-halogenoethylenes can yield compounds $CF_3{\cdot}[CF_2]_n{\cdot}[CX_2{\cdot}CY_2]{\cdot}I$ (X and Y = H, F, Cl, Br), and clearly application of the procedures described above will lead to the synthesis of a large number of fluorinated acids.

Experimental.

Preparation of Heptafluoroiodopropane.—This fluoro-iodide, b. p. 39·8°, was prepared by the interaction of trifluoroiodomethane and tetrafluoroethylene as described in Part I (and forthcoming communication).

Reaction of Heptafluoroiodopropane with Acetylene.—Heptafluoroiodopropane (3·0 g.) and acetylene (0·35 g.) were heated in a Pyrex tube of *ca.* 50 ml. capacity at 220° for 12—24 hours. Under these conditions a slight excess of acetylene was present at the end of reaction, no cuprene was formed, and the fluoro-iodide was quantitatively converted into an almost colourless liquid (3·2 g.) with b. p. >50°. The crude product (32·4 g.) from ten such experiments was distilled through an efficient fractionating

column and gave **3 : 3 : 4 : 4 : 5 : 5 : 5-*heptafluoro*-1-*iodopent*-1-*ene*** (29·2 g.), b. p. 101·5—103°/772 mm., n_D^{25} 1·381 (Found : I, 39·0; F, 41·0%; *M*, 316. $C_5H_2IF_7$ requires I, 39·4; F, 41·3%; *M*, 322).

Oxidation of **3 : 3 : 4 : 4 : 5 : 5 : 5-*Heptafluoro*-1-*iodopent*-1-*ene*.**—The fluoroiodopentene (4·0 g.) was sealed in a Carius tube with potassium permanganate (8·0 g.), potassium hydroxide (4·0 g.), and water (40 ml.), and was shaken vigorously whilst heated to 85—90°. After 2 hours the products from two such tubes were combined and examined. Heptafluoropropane (0·1 g.; *M*, 170) was stored for further examination (see below). The aqueous solution was treated with sulphur dioxide, acidified with sulphuric acid, and extracted with ether. After the ether had been removed through a Vigreux column, the residual acid was neutralised to bromothymol-blue with potassium hydroxide, and the solution evaporated to dryness. The solid obtained by extraction with hot absolute alcohol, followed by removal of the alcohol, was cooled and treated with concentrated sulphuric acid. Distillation through a short column gave heptafluorobutyric acid (2·65 g., 51%).

In two further experiments a total of 32 g. of the fluoroiodopentene was oxidised by the addition of old potassium permanganate (30 g.), portionwise during 2 hours, to the fluoro-iodide (16 g.), potassium hydroxide (4 g.), and water (40 ml.) in a flask fitted with reflux condenser, and shaken vigorously in a vibro-shaker. Three further portions of potassium hydroxide (4 g.) and water (40 ml.) were added during the reaction. The reaction temperature (thermometer in the liquid) was kept at 60°. The volatile products of reaction were condensed in a trap cooled by liquid air. Heptafluorobutyric acid (13·5 g., 83%) was isolated from the reaction product as described above. The total fluoro-acid prepared (16·15 g.) was distilled through a 15-plate column, to yield pure heptafluorobutyric acid (Found : C, 22·2; H, 0·7%; equiv., 213·8. Calc. for $C_4HO_2F_7$: C, 22·4; H, 0·5%; equiv., 214·0).

Properties of Heptafluorobutyric Acid.—Heptafluorobutyric acid is a colourless liquid, b. p. 120·8—121·0°, n_D^{25} 1·295, which fumes in air and is soluble in water, ethanol, acetone, ether, benzene, and carbon tetrachloride.

The volatile product of the oxidation was heptafluoropropane (1·2 g., 7%) (Found : *M*, 170. Calc. for C_3HF_7 : *M*, 170), b. p. −17°. Brice, Pearlson, and Simons (*J. Amer. Chem. Soc.*, 1946, **68**, 968) report b. p. −21°. After combination with the material obtained earlier (1·3 g. total), it was brominated thermally by passage of a mixture with excess of bromine vapour through a 45-cm. Pyrex tube, packed with short lengths of Pyrex tubing, at 620°. The product was washed with dilute alkali, fractionated *in vacuo*, and shown to be bromoheptafluoropropane (93% yield) (Found : C, 14·2%; *M*, 249. Calc. for C_3BrF_7 : C, 14·45%; *M*, 249), b. p. 12°. Brice, Pearlson, and Simons (*loc. cit.*) report b. p. 11—12°.

Reactions and Derivatives of Heptafluorobutyric Acid.—Piperazine (0·1 g.) was dissolved in the minimum amount of water and added to heptafluorobutyric acid (0·4 g.). Ether was added and the solid was removed by filtration and recrystallised from ethanol, to yield *piperazinium bisheptafluorobutyrate* (0·3 g.), m. p. 247° (decomp.) (Fisher hot plate) (Found : C, 28·3; H, 2·6; N, 5·3. $C_{12}H_{12}O_4N_2F_{14}$ requires C, 28·0; H, 2·3; N, 5·45%).

Benzylamine heptafluorobutyrate (0·15 g.), m. p. 100—102°, was prepared from benzylamine (0·1 g.) and heptafluorobutyric acid (0·2 g.) in ethereal solution and was recrystallised from benzene (Found : C, 41·7; H, 3·1. $C_{11}H_{10}O_2NF_7$ requires C, 41·1; H, 3·1%).

A freshly prepared solution (6%) of nitron in aqueous acetic acid (10%) was slowly added to a solution of heptafluorobutyric acid (0·1 g.) in water; the precipitate was removed by filtration and recrystallised several times from aqueous ethanol, to give *nitron heptafluorobutyrate* (Found : N, 10·5. $C_{24}H_{17}O_2N_4F_7$ requires N, 10·65%).

Mercuric oxide dissolved in a slight excess of heptafluorobutyric acid (0·5 g.) during 48 hours, giving a viscous solution which, when left in a vacuum-desiccator for 2 weeks, yielded *mercuric heptafluorobutyrate* (Found : C, 15·3. $C_8O_4F_{14}Hg$ requires C, 15·3%), a white solid, very soluble in water in which it is appreciably hydrolysed. When heated in aqueous solution it yielded a basic salt.

Heptafluorobutyric acid (3·0 g.) was kept at room temperature for 12 hours in a 10% excess of ethyl alcohol and concentrated sulphuric acid (0·2 ml.), then heated under reflux for 3 hours. Ice-water was added and the ester layer taken into a vacuum system where it was dried. When removed from the system and distilled, *ethyl heptafluorobutyrate* (3·01 g., 88%) (Found : C, 30·2; H, 2·6. $C_6H_5O_2F_7$ requires C, 29·75; H, 2·05%) had b. p. 94·5—95°, n_D^{25} 1·301, n_D^{15} 1·306.

A solution of ethyl heptafluorobutyrate (2·80 g.) in anhydrous ether was cooled in ice and saturated with dry ammonia. Evaporation at room temperature, and recrystallisation of the residual solid from aqueous ethanol or chloroform, followed by sublimation at 80°/760 mm., gave *heptafluorobutyramide*, m. p. 102—103° (2·20 g., 89%) (Found : C, 22·6; H, 1·1; N, 6·6. $C_4H_2ONF_7$ requires C, 22·5; H, 0·9; N, 6·6%).

The amide (2·10 g.) was mixed with a large excess of phosphoric oxide and carefully heated. The volatile products were collected in a trap cooled in liquid air and transferred to the vacuum system. Fractionation gave *heptafluorobutyronitrile* (1·71 g., 89%) (Found : N, 7·4%; *M*, 195. C_4NF_7 requires N, 7·2%; *M*, 195), b. p. 1°/757 mm.

Heptafluorobutyronitrile (1·5 g.) was readily hydrolysed by aqueous potassium hydroxide, and evaporation and purification by extraction with absolute ethanol gave *potassium heptafluorobutyrate* (1·7 g.) (Found : K, 15·5. $C_4O_2F_7K$ requires K, 15·5%). The potassium salt (1·6 g.) was converted into *silver heptafluorobutyrate* (1·8 g.) by dissolution in water, addition of excess of 50% silver nitrate, extraction with ether, evaporation of the ether, and drying *in vacuo* (Found : Ag, 33·5. $C_4O_2F_7Ag$ requires Ag, 33·6%).

Heptafluorobutyric acid (2·0 g.), heated with excess of phosphoric oxide, gave *tetradecafluorobutyric anhydride* (1·8 g., 94%) [Found : *M* (Regnault bulb), 410; equiv., 204·8. $C_8O_3F_{14}$ requires *M*, 410;

equiv., 205·0], b. p. 108°, n_D^{24} 1·287, n_D^{β} 1·282. The molecular weight of the anhydride is normal and indicates that it is not associated in the vapour state.

Tetradecafluorobutyric anhydride (0·2 g.) was added to β-naphthol (0·06 g.) and anhydrous sodium heptafluorobutyrate (0·1 g.) in a small tube which was sealed and heated at 100° for 20 minutes. The clear liquid crystallised on cooling and, after removal of excess of anhydride and acid by evacuation, was extracted with dry light petroleum. Evaporation and sublimation of the residual solid gave *β-naphthyl heptafluorobutyrate*, (0·1 g.), m. p. 58°. Hydrolysis with sodium hydroxide and back-titration with hydrochloric acid (cf. Bourne, Tatlow, and Tatlow, *J.*, 1950, 1367) gave the heptafluorobutyryl content (Found: C_3F_7·CO, 57·5. $C_{14}H_7O_2F_7$ requires C_3F_7·CO, 57·9%).

Heptafluorobutyric acid (2·0 g.) was gently heated with excess of phosphoric pentachloride in a small flask to which was attached a fractionating column. The temperature was slowly raised until *heptafluorobutyryl chloride* (2·05 g., 97%) was obtained (Found: C, 20·6; Cl, 15·1%; *M*, 231. C_4OClF_7 requires C, 20·6; Cl, 15·3%; *M*, 232·5), b. p. 39°, n_D^{β} 1·291. With ammonia, heptafluorobutyryl chloride gave heptafluorobutyramide.

Heptafluorobutyryl chloride (0·2 g.) was added to excess of aniline in benzene (2 ml.). After filtration, the benzene solution was washed with water and evaporated to dryness at room temperature. The residual solid was purified by sublimation at 80°/760 mm., followed by recrystallisation from aqueous ethanol. *Heptafluorobutyranilide* (0·1 g.) had m. p. 92—93° (Found: C, 42·0; H, 2·5. $C_{10}H_6ONF_7$ requires C, 41·5; H, 2·1%).

By the procedure described above, excess of benzylamine yielded *N-benzylheptafluorobutyramide* (0·1 g., from 0·2 g. of chloride) (Found: N, 4·3; F, 43·3. $C_{11}H_8ONF_7$ requires N, 4·6; F, 43·9%), m. p. 55—56°, sublimes 80°/760 mm.

THE UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, July 17th*, 1950.]

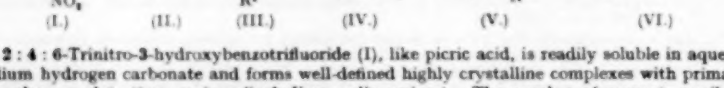
---

538. *Organic Fluoro-compounds. Part III. 2 : 4 : 6-Trinitro-3-hydroxybenzotrifluoride—a New Reagent for the Characterisation of Amines and Pyranol Bases.*

By W. B. WHALLEY.

The nitration of *m*-hydroxybenzotrifluoride gives 2 : 4 : 6-trinitro-3-hydroxybenzotrifluoride, a compound which shows considerable possibilities as a reagent for the characterisation of amines and pyranol bases.

In Part I (*J.*, 1949, 3016) it was recorded that the nitration of *m*-hydroxybenzotrifluoride gave rise to a complex mixture of nitrophenols. However, it has now been shown that vigorous nitration with fuming nitric acid readily furnishes 2 : 4 : 6-trinitro-3-hydroxybenzotrifluoride (I), unaccompanied by easily detectable quantities of other nitrophenols. The orientation of (I) was initially inferred by analogy with the behaviour of *m*-hydroxybenzoic acid which contains an electronic system comparable with that present in *m*-hydroxybenzotrifluoride and gives rise to 2 : 4 : 6-trinitro-3-hydroxybenzoic acid under similar nitration conditions (Wolffenstein and Paar, *Ber.*, 1913, **46**, 598). Because of the resistance of the trifluoromethyl group in (I) to hydrolysis with concentrated acid and alkali the orientation was established from the production of (I) by the nitration of 2-nitro-3-hydroxybenzotrifluoride (II), 4-nitro-3-hydroxybenzotrifluoride (III; $R^1 = NO_2$, $R^2 = OH$) (De Brouwer, *Bull. Soc. chim. Belg.*, 1930, **38**, 298), and 2-nitro-5-hydroxybenzotrifluoride (IV) (Part I, *loc. cit.*). Phenols (II) and (III; $R^1 = NO_2$, $R^2 = OH$) were characterised as the *p*-nitrobenzoates.



(I.) (II.) (III.) (IV.) (V.) (VI.)

2 : 4 : 6-Trinitro-3-hydroxybenzotrifluoride (I), like picric acid, is readily soluble in aqueous sodium hydrogen carbonate and forms well-defined highly crystalline complexes with primary, secondary, and tertiary amines (including cyclic amines). The number of reagents available for the characterisation of primary and secondary amines is considerable, but very few are suitable for use with tertiary amines, particularly in aqueous solution (compare "Organic Reagents for Organic Analyses," 1944, London, p. 24). The trinitrohydroxybenzotrifluoride

(I) with amines readily gives derivatives which in most cases have melting points (see Table) appreciably different from those of the corresponding picrates.

The number of salts preparable from pyranol bases for characterisation is also rather limited. With the selection of pyranol bases examined the reagent readily furnishes, in good yield, highly crystalline derivatives of type (VI) which in general exhibit only moderate solubility in solvents. Unlike picric acid, this reagent does not appear readily to form solid complexes with hydrocarbons or with ethers.

The catalytic reduction of 4-nitro-3-aminobenzotrifluoride (III; $R^1 = NO_2$, $R^2 = NH_2$) gave rise to 3 : 4-diaminobenzotrifluoride (III; $R^1 = R^2 = NH_2$) characterised by the formation of the 2 : 3-diphenylquinoxaline (V).

Experimental.

2 : 4 : 6-*Trinitro*-3-*hydroxybenzotrifluoride* (I).—*m*-Hydroxybenzotrifluoride (10 g.) was added during 15 minutes to stirred fuming nitric acid (30 ml.) without cooling. A vigorous reaction occurred and on its being kept some product crystallised. 24 Hours later the mixture was poured on crushed ice (50 g.), and the crystalline precipitate collected and washed with ice-cold water (100 ml.). 2 : 4 : 6-*Trinitro*-3-*hydroxybenzotrifluoride* (7 g.) separated from benzene in colourless rhombic plates, m. p. 88°, containing benzene of crystallisation which rapidly vaporised when the crystals were exposed to the atmosphere. Crystallisation from ethyl acetate–light petroleum gave the product in rhombic prisms, m. p. 122° (Found: C, 28·6; H, 0·8; N, 15·3; F, 19·4. $C_7H_2O_7N_3F_3$ requires C, 28·3; H, 0·7; N, 14·2; F, 19·2%). The compound is sparingly soluble in water to a yellow solution, soluble in aqueous sodium carbonate and sodium hydrogen carbonate with the evolution of carbon dioxide, easily soluble in ethyl acetate, alcohol, and acetone, moderately soluble in benzene, and very sparingly soluble in light petroleum.

2- and 4-Nitro-3-aminobenzotrifluorides were obtained by the nitration of *m*-acetamidobenzotrifluoride with acetyl nitrate (Rouche, *Bull. Acad. roy. Belg. Classe Sci.*, 1927, **13**, 346), and were subsequently converted into the corresponding nitrophenols by prolonged hydrolysis with 6*N*-sodium hydroxide solution (De Brouwer, *Bull. Soc. chim. Belg.*, 1930, **39**, 298). 2-Nitro-3-hydroxybenzotrifluoride (II) gave a p-*nitrobenzoate* which separated from aqueous methyl alcohol in slender prisms, m. p. 130° (Found: N, 8·1. $C_{14}H_7O_6N_2F_3$ requires N, 7·9%). 4-Nitro-3-hydroxybenzotrifluoride (III; $R^1 = NO_2$, $R^2 = OH$) furnished a p-*nitrobenzoate* in clusters of stout prisms, m. p. 103°, from aqueous methyl alcohol (Found: N, 7·5. $C_{14}H_7O_6N_2F_3$ requires N, 7·9%). The nitration of 2-nitro-3-hydroxy-, 4-nitro-3-hydroxy-, and 2-nitro-5-hydroxy-benzotrifluoride (Part I, *loc. cit.*) with fuming nitric acid by this method readily gave rise, in each case, to 2 : 4 : 6-trinitro-3-hydroxybenzotrifluoride, the product from each preparation being identical with the others and with that from *m*-hydroxybenzotrifluoride.

The Characterisation of Amines.—The reagent is conveniently employed in saturated aqueous or alcoholic solution and on admixture with an aqueous or alcoholic solution of the amine the crystalline derivative separates rapidly, and is collected and recrystallised, usually from alcohol or aqueous alcohol containing about 0·5% of the reagent, until of constant m. p. One recrystallisation is usually sufficient. Occasionally the use of a benzene solution of the reagent and amine is more convenient (where the latter is easily available in the anhydrous condition). The Table records details of a series of amine derivatives.

Characterisation of Pyranol Bases.—An excess of a saturated alcoholic solution of the reagent is added to a solution of the pyranol base in the same solvent. The crystalline salt separates immediately and is recrystallised from methyl or ethyl alcohol containing about 0·5% of the reagent.

The pyranol bases required for the preparation of the derivatives described were obtained from the corresponding chlorides by standard methods. The chlorides were prepared by the condensation in ethyl acetate of the appropriate acetophenone and *o*-hydroxy-aldehyde in the presence of dry hydrogen chloride.

The following pyrylium *trifluoromethylpicrates* were so prepared (all crystallised from methanol; those marked * exhibited rather sparing solubility; the temperatures given in parenthesis after the m. p. indicate the point at which darkening was first observed): **7-hydroxy-2-phenylbenzopyrylium*, shimmering red-brown plates with a green reflex, m. p. 236–238° (decomp.) (180°) (Found: C, 51·5; H, 2·4; N, 8·1; F, 10·1. $C_{22}H_{12}O_9N_3F_3$ requires C, 50·9; H, 2·3; N, 8·1; F, 11·0%); **7-hydroxy-2-p-tolylbenzopyrylium*, shimmering red-brown plates exhibiting a green reflex, m. p. 220–222° (decomp.) (170°) (Found: C, 52·7; H, 2·9; N, 8·1; F, 10·2. $C_{23}H_{14}O_9N_3F_3$ requires C, 51·8; H, 2·6; N, 7·9; F, 10·8%); **7-hydroxy-5-methyl-2-p-tolylbenzopyrylium*, shimmering orange-red plates, m. p. 207° (decomp.) (200°) (Found: C, 52·0; H, 3·0; N, 7·8; F, 10·1. $C_{24}H_{16}O_9N_3F_3$ requires C, 52·6; H, 2·9; N, 7·7; F, 10·4%); **7-hydroxy-2-phenyl-5-methylbenzopyrylium*, shimmering red-brown plates with a green sheen, m. p. 220–222° (decomp.) (Found: C, 51·4; H, 2·5; N, 8·1; F, 10·2. $C_{23}H_{14}O_9N_3F_3$ requires C, 51·8; H, 2·6; N, 7·9; F, 10·7%); *6-methoxy-2-phenylbenzopyrylium*, green-brown silky needles, m. p. 178° (decomp.) (164°) (Found: C, 50·8; H, 3·3; N, 8·4; F, 10·2. $C_{23}H_{14}O_{10}N_3F_3,0{\cdot}5H_2O$ requires C, 50·9; H, 2·8; N, 7·9; F, 10·5%); *6-methoxy-2-p-tolylbenzopyrylium*, orange-brown silky needles which changed on being kept in contact with the solvent to glistening, slender, almost black parallelograms with a green sheen, m. p. 160–163° (decomp.) (Found: C, 52·5; H, 2·5; N, 7·9; F, 9·7. $C_{24}H_{16}O_9N_3F_3$ requires C, 52·6; H, 2·9; N, 7·7; F, 10·4%); *7-hydroxy-2-phenyl-5:6-dimethylbenzopyrylium*, rosettes of red-brown needles, m. p. 241–243° (decomp.) (220°) (Found: C, 53·0; H, 3·3; N, 7·4; F, 9·7. $C_{24}H_{16}O_9N_3F_3$ requires C, 52·6; H, 2·9; N, 7·7; F, 10·4%); **7-hydroxy-2-p-tolyl-5:6-dimethylbenzopyrylium*, greenish-brown shimmering plates, m. p. 243–244° (decomp.) (220°) (Found: C, 52·4; H, 3·2; N, 7·4; F, 9·6. $C_{25}H_{18}O_9N_3F_3,0{\cdot}5H_2O$ requires C, 52·6; H, 3·3; N, 7·5; F, 10·0%); **7-methoxy-6-ethoxy-2-p-tolylbenzopyrylium*, greenish-brown needles, m. p. 182–185° (decomp.) (Found: C, 51·3; H, 3·6; N, 7·3; F, 8·7,

$C_{18}H_{20}O_{10}N_2F_2,H_2O$ requires C, 51·3; H, 3·6; N, 6·9; F, 9·4%); and *6 : 7-*dimethoxy-2-p-tolylbenzopyrylium*, glistening greenish-brown stout tablets, m. p. 184—185° (decomp.) (180°) (Found: C, 51·7; H, 3·1; N, 7·3; F, 9·1. $C_{32}H_{14}O_{10}N_2F_2$ requires C, 52·0; H, 3·1; N, 7·3; F, 9·9%).

Amine.	M. p. of derivative.	M. p. of picrate.[4]	Crystalline form.	Formula.	Found, %. N.	Found, %. F.	Requires, %. N.	Requires, %. F.
Aniline	182—183° (decomp.)	165°	Yellow slender needles [2]	$C_{13}H_9O_7N_4F_3$	14·5	14·1	14·4	14·6
Quinoline	203	203	Deep-yellow slender needles [1]	$C_{14}H_9O_7N_4F_3$	13·1	12·8	13·1	13·4
Morpholine	238—242 (decomp.)	146	Pale yellow massive tablets [1]	$C_{11}H_{11}O_8N_4F_3$	14·2	14·5	14·4	14·7
Pyridine	179	167	Bright-yellow slender prisms [1]	$C_{13}H_9O_7N_4F_3$	14·6	15·2	14·9	15·2
n-Butylamine	156	151	Yellow massive long prisms [1]	$C_{11}H_{13}O_7N_4F_3$	14·8	15·3	15·1	15·4
*iso*Propylamine	157	—	Bright-yellow long flat prisms [3]	$C_{10}H_{11}O_7N_4F_3$	15·9	15·8	15·7	15·7
Triethylamine	93	173	Yellow short stout pale prisms [3]	$C_{12}H_{17}O_7N_4F_3$	13·9	14·3	14·1	14·3
o-Toluidine	171	185	Straw-coloured slender needles [3]	$C_{14}H_{11}O_7N_4F_3$	13·8	14·1	13·9	14·1
Dimethylaniline	165	162	Pale yellow stout tablets [2]	$C_{15}H_{13}O_7N_4F_3$	13·7	13·4	13·3	13·6
Diethylamine	113	—	Bright-yellow short stout tablets [3]	$C_{11}H_{13}O_7N_4F_3$	15·2	15·0	15·1	15·4
Lepidine	202	212	Orange-yellow plates [1]	$C_{17}H_{11}O_7N_4F_3$	12·6	12·7	12·8	12·9
Benzidine	250—252 (decomp.)	—	Rosettes of yellow stout prisms [3]	$C_{26}H_{16}O_{14}N_8F_6$	14·6	13·9	14·4	14·6
Diethylaniline	92	142	Greenish-yellow prisms [3]	$C_{17}H_{17}O_7N_4F_3$	13·0	11·7	12·5	12·7
4-*m*-Xylidine	183—184 (decomp.)	209	Pale yellow thin plates [3]	$C_{15}H_{13}O_7N_4F_3$	13·6	13·4	13·4	13·6
α-Naphthylamine	192 (decomp.)	161	Rosettes of pale yellow needles [3]	$C_{17}H_{11}O_7N_4F_3$	12·7	12·7	12·7	12·9
Quinaldine	198	191	Bright lemon-yellow long slender needles [1]	$C_{17}H_{11}O_7N_4F_3$	12·7	12·7	12·6	12·9

[1] Methyl alcohol containing 0·5% of the reagent used for crystallisation.
[2] Aqueous methyl alcohol containing 0·5% of the reagent used for crystallisation.
[3] Water containing 0·5% of the reagent used for crystallisation.
[4] The picrate m. p.s recorded are those given in "Organic Reagents for Organic Analyses," 1944, London.

3 : 4-*Diaminobenzotrifluoride*.—The reduction of 4-nitro-3-aminobenzotrifluoride (2·5 g.) in methyl alcohol (100 ml.) with a palladium–charcoal catalyst [from charcoal (0·5 g.) and palladium chloride (0·3 g.)] proceeded rapidly, and after evaporation of the solvent **3 : 4-***diaminobenzotrifluoride* was obtained. It crystallised from light petroleum–benzene in rosettes of small prisms, m. p. 58°. Sublimation at 140°/0·1 mm. gave rhombic plates, m. p. 58° (Found: N, 16·6. $C_7H_7N_2F_3$ requires N, 15·9%).

2 : 3-*Diphenyl-6-trifluoromethylquinoxaline*.—A solution of the diamine (0·2 g.) and benzil (0·2 g.) in methyl alcohol (5 ml.) was warmed on the steam-bath for 30 minutes and then cooled, whereupon **2 : 3-***diphenyl-6-trifluoromethylquinoxaline* (V) (0·2 g.) separated; it crystallised from methyl alcohol in shimmering, colourless, rectangular plates, m. p. 127° (Found: N, 8·3. $C_{21}H_{13}N_2F_3$ requires N, 8·0%).

The author thanks Imperial Chemical Industries Limited (General Chemicals Division) for a generous gift of benzotrifluoride.

UNIVERSITY OF LIVERPOOL. [*Received, May 16th*, 1950.]

539. *The Formation and Constitution of the Perchromates.*

By Abraham Glasner.

Evidence is brought forward that the formulæ of the blue and the violet perchromate correspond to those given by Riesenfeld *et al.*. It is suggested that the ether-soluble blue perchromate is formed by addition of an HO_3 radical to chromium trioxide: $CrO_3 + HO_3 \rightleftharpoons HCrO_6$.

At a pH above 4·5, or on the addition of an excess of hydrogen peroxide, by which a reduction in the concentration of the chromic acid and consequently a rise in the pH is produced, the blue perchromate adds another molecule of hydrogen peroxide forming the violet perchromate: $HCrO_6 + H_2O_2 \rightleftharpoons H_3CrO_7$.

The quinquevalency of the chromium in the perchromates and the reduction of chromic acid by hydrogen peroxide in acid solution is thus considered to be due to the odd electron in the HO_3 radical. It is also considered that this radical is present in all hydrogen peroxide solutions owing to the equilibrium $3H_2O_2 \rightleftharpoons 2HO_3 + 2H_2O$.

Riesenfeld *et al.* (*Ber.*, 1905, **38**, 1885, 3380, 3578, 4068; 1908, **41**, 2826, 3536, 3941; 1914, **47**, 548) established that there are three series of perchromates which may be distinguished by their colours as blue, violet, and red, and may be represented by the typical formulæ $PyHCrO_6$ (Py = pyridine), KH_3CrO_7, and K_3CrO_8. The valency of these compounds is rather perplexing; Riesenfeld ascribed to them first septi- and later quinque-valency (" Lehrbuch der anorganischen Chemie," 1939, 2nd edn., p. 518).

Schwarz and Giese (*Ber.*, 1932, **65**, 871; 1933, **66**, 310; 1936, **69**, 575) concluded, on the evidence of oxidation power, that the pyridine complex is an addition compound of CrO_3 (the well-known, blue, ether-soluble perchromate), and that the formulæ of the other perchromates should be doubled ($K_4Cr_2O_{12}.2H_2O$ and $K_4Cr_2O_{14}$), attributing sexivalency to each of these per-compounds. On the other hand, the *X*-ray diffraction (Wilson, *Arkiv Kemi, Min. Geol.*, 1941, **15**, *B*, No. 5, 7), the magnetic moment (Tjabbes, *Z. anorg. Chem.*, 1933, **210**, 385), and the isomorphism of the red perchromate K_3CrO_8 with K_3TaO_8 (Böhm, *Z. Krist.*, 1926, **63**, 319) indicate that the chromium in this case, at least, is quinquevalent and that the compound should be formulated as $K_3Cr(O_2)_4$. The constitution of the perchromates is therefore still in doubt and they are given quite different formulæ by various authors (Ephraim, " Inorganic Chemistry," 5th edn., p. 525).

Bobtelsky, Glasner, and Bobtelsky-Chaikin (*J. Amer. Chem. Soc.*, 1945, **67**, 966) reported the results of photometric measurements on the catalytic decomposition of hydrogen peroxide by chromic acid, and it is the purpose of the present paper to apply these and other data to the problem of the perchromates.

Experimental.

The Blue Perchromate.—When chromic acid is mixed with hydrogen peroxide in 80% ethyl alcohol at 0°, a blue colour develops which attains a maximum intensity after several minutes and then remains almost constant for some time. This stability had been noted by Wiede (*Ber.*, 1897, **30**, 2178; 1898, **31**, 516, 3139; 1899, **32**, 378), and in our experiments, too, scarcely any bubbles of oxygen were observed.

Measurements were made with a Hellige " panphotometer " and three colour filters, 530, 550, and 570 mμ., which showed slightly increasing extinctions in the order written. The extinction values of chromic acid solutions measured at these wave-lengths were small and were subtracted from the actual readings. The constant ratio of the three values thus obtained served as a control on the accuracy of the measurements as well as on any change in the hue of the solutions (for experimental details, see *J. Amer. Chem. Soc.*, *loc. cit.*). Tables I and II show the maximum extinctions E (for a 10-mm. layer at 550 mμ.), as well as the equilibrium constants K_1, calculated as explained below, of two series of solutions containing various proportions of the reactants. From Table I, it may be seen that the extinction of the blue perchromate (Per), formed at a constant initial concentration of hydrogen peroxide in excess

Table I.*

Solutions: x ml. of 0·02069M-CrO_3 + 5 ml. of 0·0637M-H_2O_2 + 40 ml. of 96% EtOH + $(5 - x)$ ml. of H_2O.

x.	10^3E.	$\frac{[CrO_3]}{[Per]}$.	$10^3[H_2O_2]$.	10^3K_1.	x.	10^3E.	$\frac{[CrO_3]}{[Per]}$.	$10^3[H_2O_2]$.	10^3K_1.
1	260	0·115	5·81	5·09	3 †	768	0·134	4·73	4·36
2	506	0·146	5·29	5·62		(758)	(0·149)		(4·80)
	(516)	(0·124)		(4·77)	4	980	0·184	4·27	5·13
						(990)	(0·172)		(4·80)
								Mean	(5·05)

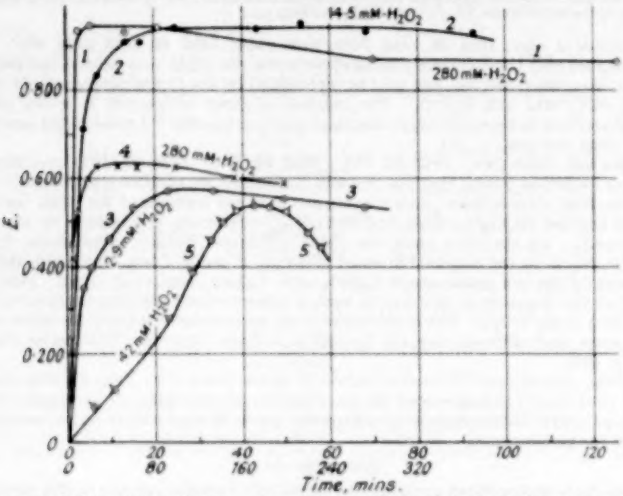
* For significance of data in parentheses, see p. 2796.
† 3 Ml. $CrO_3 = 1·241 \times 10^{-3}$M.

TABLE II.

$10^3[H_2O_2]_0$.	10^3E.	$[CrO_3]$. [Per]	$10^3[H_2O_2]$.	10^3K_1.	$10^3[H_2O_2]_0$.	10^3E.	$[CrO_3]$. [Per]	$10^3[H_2O_2]$.	10^3K_1.
1·450	310	2·06	0·787	4·55	5·248	780	0·218	3·578	4·66
2·900	568	0·672	1·684	4·65	5·800	815	0·166	4·056	4·29
3·496	640	0·484	2·126	4·74	8·700	880	0·080	6·816	4·48
4·374	723	0·314	2·826	4·71				Mean	4·63

is proportional to the concentration of the chromic acid. The initial concentration of the chromic acid in the series of solutions presented in Table II was kept constant at $1{\cdot}3536 \times 10^{-4}$M-$CrO_3$ and that of the hydrogen peroxide ($[H_2O_2]_0$) was varied, as shown. There is a steady increase in the extinction, which attains a maximum of $E = 0{\cdot}950$ (for a 10-mm. layer of solution) at a molecular ratio of hydrogen peroxide to chromic acid of about 12 : 1 (see also figure). On further increase in the concentration of hydrogen

Extinction–time curves of blue and violet perchromates in 80% alcoholic solution.



Curves 1, 2, 3 *for* 1·3536mM-CrO_3. *Curves* 4, 5 *for* 1·2094mM-$Na_2Cr_4O_7$ (*lower time scale*).

peroxide, even to 100-fold excess, the extinctions at 530 and 550 mμ. did not change, but those at 570 mμ. decreased; at the same time the solutions acquired a slight violet tint, indicating the presence of the violet perchromate. (The violet perchromate has a slightly higher extinction at 530 mμ. than at 550 mμ., and its optical density at 570 mμ. is low.) This should have been expected, for, with the consumption of the chromic acid the pH of the solution rises, creating conditions necessary for the formation of the violet perchromate. Therefore, it was assumed that in solutions containing more than 12-fold excess of hydrogen peroxide, the chromic acid initially present has been converted quantitatively into the blue perchromate and the extinction measured was that of a blue $1{\cdot}3536 \times 10^{-4}$ M-perchromate solution.

Next, the value of x in the assumed equilibrium $CrO_3 + xH_2O_2 \rightleftharpoons CrO_3.(H_2O_2)_x$ was found by trial to be equal to 1·5, yielding the constants:

$$K_1 = [CrO_3][H_2O_2]^{1.5}/[Per] = 4{\cdot}63 \times 10^{-3} \text{ (mean)},$$

as shown in the tables; [Per] is the molar concentration of the blue perchromate as calculated from the extinction measured, $[CrO_3]$ the initial concentration of chromic acid less the fraction converted into the per-compound, $[H_2O_2]$ the initial concentration of hydrogen peroxide less one and a half times the concentration of the per-compound in moles.

Large deviations from the average, especially in Table I, were obtained in solutions containing a relatively big excess of hydrogen peroxide. These may be accounted for by experimental mistakes in the photometric readings (±0·01E) as shown by the corrected data given in Table I in parentheses.

The Violet Perchromate.—It was proved in our previous paper (*loc. cit.*) that in dichromate solutions, or generally in solutions above pH 4·5, the violet perchromate is formed. When the reagents are mixed in alcoholic solutions in this case, too, extinction–time curves showing maxima were obtained, but the attainment of these maxima took rather a long time even at 18° (1—2·5 hours). Meanwhile the hydrogen peroxide decomposed and some of the alcohol was oxidised to acetaldehyde, though no evolution of oxygen

was observed. Therefore the concentration of the hydrogen peroxide at the point of maximum extinction cannot be calculated, though the symmetry of the extinction curves allows one to assume that just half of the original amount of hydrogen peroxide has been consumed.

Treating a $1{\cdot}2094 \times 10^{-4}$M-sodium dichromate solution in 80% alcohol with a very large excess (100-fold) of hydrogen peroxide, and measuring the extinction of a 5-mm. layer with a 530 mμ. filter, gave the value $E = 0{\cdot}632$. This extinction did not increase on a further addition of hydrogen peroxide and remained constant for a long time, giving, unlike the solution with lower concentrations of hydrogen peroxide, an extinction–time curve with a steady maximum; the figure shows a number of typical curves. Therefore it was assumed that this is the extinction of the violet perchromate corresponding to the above concentration of dichromate.

The $E_{max.}$ values of two series of solutions (the concentration of dichromate being varied in one case, and that of hydrogen peroxide in the other), together with the calculated equilibrium constants K_1, are given in Tables III and IV.

TABLE III.

$4{\cdot}200 \times 10^{-4}$M-$H_2O_2$; 18°.

$10^4[Na_2Cr_2O_7]_t$.	E.	$\frac{[Cr_2O_7'']^{0{\cdot}4}}{100[Per]^2}$.	K_1.
1·2094	0·550	113	0·723
1·8141	0·720	110	0·703
2·4188	0·850	106	0·681
3·0235	0·938	109	0·695
3·6282	1·010	110	0·705
		Mean	0·702

TABLE IV.

$2{\cdot}4188 \times 10^{-4}$M-$Na_2Cr_2O_7$; 18°.

$10^4[H_2O_2]_t$.	E.	K_1.
2·657	0·526	0·754
4·212	0·830	0·735
5·616	0·995	0·827
7·020	1·135	0·768
	Mean	0·752

As may be seen in Table III, a 3-fold increase in the concentration of the dichromate less than doubles the extinctions. This suggests that the reaction with the hydrogen peroxide is preceded by dissociation of the dichromate. This surmise is confirmed by the constancy of the quotient $[Cr_2O_7'']^{0{\cdot}4}/[Per]^2$, indicating, also, that the oxidation of the alcohol is bimolecular with respect to the violet perchromate.

At the point of maximum extinction, the velocity of formation of the violet perchromate and the velocity of its reduction by ethanol are equal; therefore the expression $[Cr_2O_7'']^{0{\cdot}4}[H_2O_2]^x/[Per]^2 = K_1$ should be a constant. From this equation x was obtained by trial. With $x = 2{\cdot}5$, the constants K_1 shown in the tables were obtained. (As the exact concentration of hydrogen peroxide is unknown, it has been assumed to have been reduced to half of its initial value in each case.)

The relation between the perchromates obtained from dichromate and from chromic acid is illustrated by the following qualitative experiment. On addition of a calculated amount of 0·1N-sodium hydroxide in 80% alcohol to a blue alcoholic solution of perchromic acid, the solution becomes violet in a few seconds without any noticeable evolution of oxygen, although the direct formation of the violet perchromate would require a few hours. Further, on neutralization of the sodium hydroxide by an equivalent amount of an alcoholic solution of hydrochloric acid, the blue colour reappears almost instantaneously. If the experiment is carried out at 0° these titrations can be repeated for several hours, always with the same results, until the hydrogen peroxide is entirely decomposed. Also there is no difference whether the "titration experiment" is started with a violet solution obtained from dichromate or with a blue solution obtained from chromic acid. These experiments leave no doubt that the two perchromates can be interconverted just by changing the hydrogen-ion concentration of the solution, without the intermediate formation of chromic acid.

DISCUSSION.

The extinction values of the alcoholic solutions measured and the equilibrium constants K_1 show that the blue perchromate is formed from one molecule of chromic acid and 1½ molecules of hydrogen peroxide. This may be expressed by the equation $2CrO_3 + 3H_2O_2 \rightleftharpoons 2HCrO_4 + 2H_2O$, in agreement with the formula proposed by Wiede and Riesenfeld (*loc. cit.*). The dimeric formula $H_2Cr_2O_{12}$, or the participation of the dichromate ion, is rejected, for it has been proved by all the authors mentioned that the blue perchromate, or more exactly its pyridine compound $PyHCrO_4$, is a monomer containing only one chromium atom. Thus the strange fact that a molecule of hydrogen peroxide should be divided between two molecules of chromic acid calls for an explanation, especially as it may be the cause of the peculiar properties of the perchromates.

On neutralization, the blue perchromate is readily converted into the violet form. The smooth change of colour from blue to violet on the addition of a mild alkali had been observed by Wiede (*loc. cit.*), and later Hofmann and Hiendelmaier (*Ber.*, **1904**, **37**, 1663, 3405; **1905**, **38**, 3059, 3066) suggested that the blue colour characterizes the per-acid whilst the salts have a reddish tint. The violet perchromate is formed, as the "equilibrium constants" K_1 show, from 0·5 molecule of dichromate and 2·5 molecules of hydrogen peroxide. Therefore the difference between the blue and the violet per-compounds should be only the addition of another molecule of hydrogen peroxide: $CrO_4' + H_2O_2 \rightleftharpoons H_2CrO_5'$ (a reaction which seems to be possible only at pH above 4·5, *i.e.*, when the weak acid $HCrO_4$ is ionised).

The direct formation of the violet perchromate is comparatively slow. This may be connected with the observed participation of only half a molecule of dichromate in the reaction, indicating that the dichromate ion dissociates according to the equation $Cr_2O_7'' + 2H' \rightleftharpoons 2CrO_4 + H_2O$, and the small concentration of the chromium trioxide present at any moment is responsible for the slow reaction. Hence, there is evidence that the violet perchromate, too, is monomeric and that it contains half a molecule of hydrogen peroxide.

For the explanation of these results the dissociation of hydrogen peroxide suggests itself: $3H_2O_2 \rightleftharpoons 2H_2O + 2HO_3$. This kind of disproportionation of hydrogen peroxide in alkaline solutions has already been proposed by Calvert (*Z. physikal. Chem.*, 1901, **38**, 513). The HO_3 radicals would then add simply to the chromic acid molecules thus: CrO_3,aq. + $HO_3 \rightleftharpoons HCrO_4 + H_2O$.

The above representation is not only simple, but also explains the reduction of the chromium to the quinquevalent state by the odd electron of the HO_3 radical. Moreover, the intense coloration of the perchromate, and the analytically peculiar behaviour of the peroxidic oxygen, are also better understood.

As similar phenomena are typical for many per-compounds of the transition elements, the proposed interpretation may be quite general for this body of compounds as well as for the reducing action of hydrogen peroxide on such compounds as permanganate or ferric iron.

I thank Prof. Bobtelsky for the many fruitful discussions which helped to clarify the ideas presented in this paper.

THE HEBREW UNIVERSITY, JERUSALEM, ISRAEL. [*Received, April* 11th, 1950.]

---

540. *Reactions of Organic Peroxides. Part III. Oxidation of Methylcyclopentane and Methylcyclohexane.*

By E. J. GASSON, E. G. E. HAWKINS, A. F. MILLIDGE, and D. C. QUIN.

Liquid-phase oxidation of methyl*cyclo*pentane and methyl*cyclo*hexane at 100—130° under pressure yields some hydroperoxides, but continuation of the oxidation beyond a limited stage causes rapid decomposition of the peroxides and formation of alcohols, ketones, acids, and lactones. Such of these products as have been identified may arise from radicals produced from the hydroperoxides.

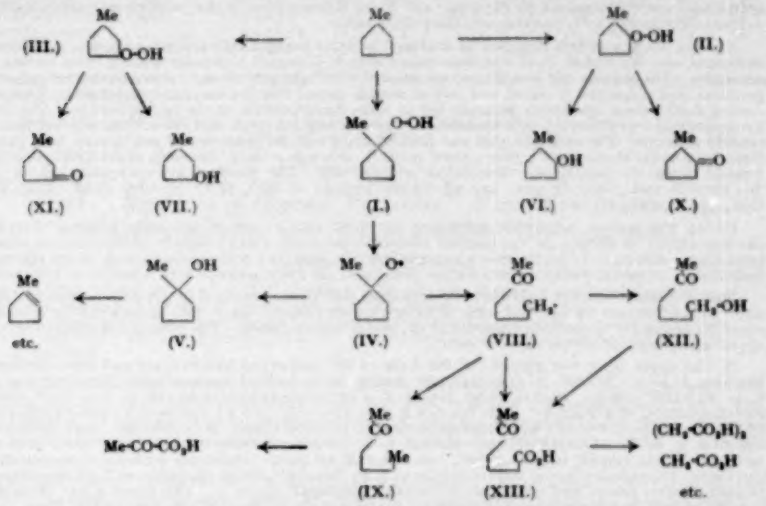
CHAVANNE and his co-workers (*inter al.*, *Bull. Soc. chim. Belg.*, 1927, **36**, 206; 1930, **39**, 206, 287; 1931, **40**, 611, 626; 1932, **41**, 209; 1933, **42**, 537) found that most of the oxidation products of many alkyl*cyclo*paraffins studied arose from attack at the tertiary carbon atom, followed by ring opening. The compounds thus formed were tertiary alcohols, ketones, keto-acids, and, in smaller amounts, degradation products formed by further oxidation. From dialkyl-substituted hydrocarbons ditertiary alcohols and diketones were similarly produced. Very probably all these products were derived from hydroperoxides first formed, although such compounds were not isolated.

The oxidation of methyl*cyclo*pentane has now been studied; the products formed confirm Chavanne's results and also include the intermediate hydroperoxide. Liquid-phase oxidations were carried out at 100—130° under pressure, with and without catalysts; varying the conditions altered little except relative amounts of the products. A hydroperoxide was first formed, but was later accompanied by increasing quantities of alcohols, ketones, lactones, and acids, until at about 8% peroxide concentration the decomposition of the hydroperoxide proceeded more rapidly than its formation. Many of the compounds isolated are accounted for in the scheme on p. 2799.

On initial oxidation the methyl*cyclo*pentane may give any of the hydroperoxides (I), (II), or (III), although it would be expected that the major product would be (I). This tertiary hydroperoxide would provide 1-methyl*cyclo*pentanol (V) *via* the radical (IV), whilst the corresponding radicals from the 2- and 3-hydroperoxides would yield 2- and 3-methyl*cyclo*pentanol (VI and VII), or 2- and 3-methyl*cyclo*pentanone (X and XI). 1-Methyl*cyclo*pentanol, 3-methyl*cyclo*pentanone, and traces of various unidentified alcohols and ketones have been found amongst the products.

Many of the oxidation products can best be accounted for by rearrangement of the radical (IV) to the radical (VIII). This can then either gain hydrogen to yield methyl *n*-butyl ketone (IX), gain a hydroxyl radical to form 6-hydroxyhexan-2-one (XII), or be further oxidised to

5-ketohexanoic acid (XIII). All three compounds have been identified in the products of oxidation. The ketohexanoic acid or methyl butyl ketone might further be oxidised (cf. Robertson and Waters, *J.*, 1948, 1574) to succinic and acetic acids or by gradual degradation yield formic acid, pyruvic acid, etc. Formic, acetic, pyruvic, and succinic acids were all found.



Lactones of unknown structure have also been found; they are probably derived from the C_5 or C_6 hydroxy-acids, and may arise by peroxidation of a ketone [cf. the reaction of perbenzoic acid with cyclic ketones (Friess, *J. Amer. Chem. Soc.*, 1949, **71**, 2571)].

The 1-hydroperoxide was obtained pure by repeated extraction with cold alkali and regeneration from the sodium salt with carbon dioxide.

From similar oxidations of methyl*cyclo*hexane the corresponding 1-hydroperoxide was obtained; the other products were not examined in detail but also appeared to consist of alcohols, ketones, and acids.

The reactions of these hydroperoxides are considered later (Parts IV and V).

Experimental.

(M. p.s are uncorr. Elementary analyses are by Drs. Weiler and Strauss. Identities of known compounds were confirmed by mixed melting point determinations.)

Methylcyclopentane.—The hydrocarbon used in these oxidation experiments was derived from (*a*) isomerisation of *cyclo*hexane with aluminium chloride (Nenitzescu and Cantuniari, *Ber.*, 1933, **66**, 1097; Glassebrook and Lovell, *J. Amer. Chem. Soc.*, 1939, **61**, 1717), and (*b*) a petroleum fraction (supplied by Anglo-Iranian Oil Co.). In both cases the methyl*cyclo*pentane, when required pure, was passed through a column of silica gel to remove aromatic compounds.

Oxidations.—In preliminary oxidation experiments at 40—50°/1 atm. absorption of oxygen was too slow. Pressure oxidation at a higher temperature were carried out batchwise and continuously in two apparatus:

(*a*) Air was introduced through a sintered-glass disc at the bottom of an electrically-heated Pyrex-glass column (5 ft. long; 1 in. in internal diameter), and the exit vapours were passed through stainless-steel cooling traps. In the continuous runs the hydrocarbon was fed in at the top of the reactor, and the product removed at the base. The temperatures were 100° to 135°, and the pressure from 50 to 75 lbs./sq. in. The peroxide content of the crude product from this apparatus rarely rose above 5—7% w/v, and, if the oxidation proceeded too far, the peroxide content fell and the acid and lactone content rose.

(*b*) The compound was stirred in a stainless-steel reactor (12 in. × 4 in.), at *ca.* 1400 revs./min. The temperature was generally 130° and pressures varied from 75 to 200 lbs./sq. in. Again the peroxide content of the crude product under the best conditions reached 7—8%, but decomposition products were also present.

Addition of sodium carbonate or metal-salt catalysts during the oxidation led to more rapid decomposition of the peroxide; the presence of magnesium oxide gave rise to the best conversion into peroxide (*ca.* 8% w/v) (cf. U.S.P. 2,430,864, 2,430,865).

1-*Methylcyclopentyl Hydroperoxide*.—The hydroperoxide was isolated from the crude oxidate in two ways: (*a*) by direct extraction with 50% sodium hydroxide solution, whereupon the sodium salt crystallised and was removed by filtration, and (*b*) by concentration of the peroxide in a climbing-film evaporator, followed by conversion into the sodium salt.

The free acids were first removed by shaking the crude product with saturated aqueous potassium carbonate, and the organic layer was then shaken with 50% sodium hydroxide solution, with cooling if necessary. The sodium salt was filtered off, washed with light petroleum to remove adsorbed organic products, and suspended in water, and carbon dioxide passed into the ice-cooled suspension. Lack of cooling during these operations generally led to some decomposition of the hydroperoxide. The free hydroperoxide was extracted with benzene, the benzene solution dried, and the solvent removed under reduced pressure. The hydroperoxide was distilled under reduced pressure and was then *ca.* 95% pure. Repetition of the above process gave a purer product, although a loss of 20—40% of the hydroperoxide resulted from its incomplete removal as sodium salt. The purified hydroperoxide had b. p. 26—28°/0·25 mm., 73·5°/19 mm., and n_D^{25} 1·4526 (Found: C, 62·7, 62·9; H, 10·5, 10·35. Calc. for $C_6H_{12}O_2$: C, 61·1; H, 10·3%).

During the sodium hydroxide extraction (*a*) there was a loss of peroxidic material through decomposition; in method (*b*) the residues contained peroxides which similarly decomposed on alkali treatment. Attempts to purify this alkali-unstable peroxide had little success owing to its thermal instability. It was probably a condensation product of the hydroperoxide with a ketone or keto-acid.

Other Oxidation Products.—(*a*) Methylcyclopentane (450 g.) was oxidised in the glass column at 120° until 45 l. of oxygen (as air) had been absorbed, cobalt stearate being used as catalyst, so that no appreciable amount of peroxide remained at the end of the oxidation. The product consisted of (i) an upper organic and (ii) a lower aqueous layer.

(i) The upper layer was stripped of the bulk of the unchanged hydrocarbon and then distilled. Fraction 1, b. p. 78—82° (11 g.), consisted mainly of unchanged hydrocarbon. From fraction 2, b. p. 82—128° (1·5 g.), methyl butyl ketone 2 : 4-dinitrophenylhydrazone, m. p. 115—117° after recrystallisation, was isolated. From fraction 3, b. p. 128—140° (4·7 g.), the same 2 : 4-dinitrophenylhydrazone, m. p. 110—113°, and 1-methylcyclopentyl phenylurethane, m. p. 89—90°, were obtained. Fraction 4, b. p. 140—148° (7 g.), yielded a 2 : 4-dinitrophenylhydrazone, which after several recrystallisations had m. p. 124—125·5°, but was still not pure; admixture with the corresponding derivative of 3-methylcyclopentanone raised the m. p. to 134—136°, whilst admixture with the derivatives of methyl butyl ketone and 2-methylcyclopentanone depressed the m. p. This fraction was probably a mixture including 3-methylcyclopentanone. Fraction 5, b. p. 60—100°/18 mm. (2·8 g.), was also a mixture, but repeated recrystallisation of the 2 : 4-dinitrophenylhydrazone yielded the slightly impure derivative, m. p. 135—138°, of 3-methylcyclopentanone (Found: C, 51·2; H, 5·0; N, 19·7. Calc. for $C_{12}H_{14}O_4N_4$: C, 51·8; H, 5·0; N, 20·15%). Fractions 6 (2·4 g.), 7 (3·3 g.), and 8 (b. p. 100—220°/16 mm.; 3·3 g.), on their analytical data, evidently contained high proportions of esters; no pure, clearly defined carbonyl derivatives could be obtained, but, after hydrolysis, the acid portion from fraction 7 (b. p. 150—170°/16 mm.) yielded 5-ketohexanoic acid 2 : 4-dinitrophenylhydrazone, m. p. 135°, and semicarbazone, m. p. 173—174°. Hydrolysis of fraction 8 provided acid material insoluble in benzene, which after recrystallisation from hot water was shown by its m. p. and equivalent to be succinic acid. The last three fractions therefore contained mixtures of ketones, acids, and esters (or lactones).

(ii) The aqueous layer was extremely acid, and was extracted with ether, to remove part of the product. The ethereal extract (iia) was fractionated, and afforded derivatives of methyl butyl ketone and 3-methylcyclopentanone. In addition, a fraction, b. p. 98—160°/18 mm. (1·3 g.), yielded probably impure dodecane-2 : 11-dione 2 : 4-dinitrophenylhydrazone, m. p. 159—161° (see Part V). Fractions, b. p. 134—150° (9·1 g.), provided 1-methylcyclopentyl phenylurethane, m. p. 88—89°, and the fraction, b. p. 142—150° (4·3 g.), further yielded a 5-ketohexyl phenylurethane, m. p. 66—67°, which was much more insoluble in light petroleum (see Part IV).

The remaining aqueous solution (iib) was hydrolysed and the aqueous solution evaporated to dryness under reduced pressure. The sodium salts were suspended in ether and treated with hydrogen chloride, the inorganic material was filtered off, and the ethereal solution evaporated and distilled. Fraction 1, b. p. 108—118°, provided *p*-bromophenacyl formate, m. p. 139—141°, whilst both fractions 1 and 2 (b. p. 118—130°) (together 3·6 g.) yielded *p*-bromophenacyl acetate, m. p. 83—84°. Fraction 3, b. p. 130—140° (0·57 g.), gave *p*-bromophenacyl pyruvate, m. p. 114—115°. No derivative was obtained from fraction 4, b. p. 140—198°; this and later fractions [especially 5 (b. p. 198—225°) (2·37 g.) and 6 (b. p. 225—240°/760 mm.) (0·54 g.)] probably contained lactones, as indicated by their low ester equivalents (170—289). Fraction 5 gave slightly impure *p*-bromophenacyl succinate, m. p. 205—208°. Fraction 6 afforded an unidentified *p*-bromophenacyl ester, m. p. 140—142°. Fraction 7, b. p. 152—194°/50 mm. (1·07 g.), on cooling gave crystals of succinic acid, m. p. 181—182°, and also *p*-bromophenacyl 5-ketohexanoate, m. p. 93—94°.

(*b*) The aqueous layers from six more carefully controlled oxidation experiments (without added catalyst) were combined. After removal of the water the product was distilled. The lower-boiling fractions (up to 170°) (33·2 g.) contained ketones similar to those recorded above, 1-methylcyclopentanol, and (mainly acetic) acid. Hydrolysis of fractions, b. p. 79—105°/16 mm. (16·0 g.), yielded mainly a product, b. p. 190—200°; titration indicated that this consisted mainly of lactones and it was not further examined. Hydrolysis of a fraction, b. p. 105—130°/16 mm. (5·6 g.), yielded 6-hydroxyhexan-2-one, a lactone, and a little succinic acid (*p*-bromophenacyl ester). Hydrolysis of fractions, b. p. 112—

180°/5 mm. (24·8 g.), gave the ketol and 5-ketohexanoic acid. The following derivatives of this acid were obtained :

		Found, %.				Calc., %.		
	M. p.	C.	H.	Br.	Formula.	C.	H.	Br.
Me·CO·[CH_2]$_4$·CO_2H,H_2O ...	35—37°	48·7	7·95	—	$C_6H_{12}O_4$	48·65	8·1	—
p-Bromophenacyl ester ...	92—92·5	51·2	4·4	25·0	$C_{14}H_{15}O_4Br$	51·4	4·6	24·5
Semicarbazone	171·5—172·5	44·7	7·2	—	$C_7H_{13}O_3N_3$	44·9	7·0	—
2 : 4-Dinitrophenylhydrazone	134—136	46·7	4·4	—	$C_{12}H_{14}O_6N_4$	46·45	4·5	—

Thanks are offered to Mr. F. E. Salt, Dr. G. H. Twigg, and Mr. G. W. Godin for many valuable discussions during this work.

THE DISTILLERS COMPANY LIMITED, RESEARCH AND DEVELOPMENT DEPARTMENT,
GREAT BURGH, EPSOM. [*Received, May 18th*, 1950.]

---

541. *Reactions of Organic Peroxides. Part IV. Reactions of Methylcyclopentyl and Methylcyclohexyl Hydroperoxides.*

By E. G. E. HAWKINS.

The decomposition of methyl*cyclo*pentyl hydroperoxide thermally and by reducing agents, acid, and alkali, as well as its condensation with ketones, have been studied. Many of the decomposition products are similar to those formed during the oxidation of methyl*cyclo*pentane (Part III). The corresponding reactions of methyl*cyclo*hexyl hydroperoxide lead to similar products.

VERY little attention appears to have been paid to the reactions of *cyclo*alkyl hydroperoxides. Milas and Perry (*J. Amer. Chem. Soc.*, 1946, **68**, 1938) obtained the perphthalate from a 70% concentrate of methyl*cyclo*hexyl hydroperoxide, prepared by reaction of hydrogen peroxide with methyl*cyclo*hexyl hydrogen sulphate, and the same hydroperoxide has been produced by oxidation of methyl*cyclo*hexane itself by Ivanov and Savinova (*Doklady Akad. Nauk. S.S.R.*, 1948, **59**, 493) and reduced to the carbinol with zinc and acetic acid. The isolation of several substituted cyclic paraffin hydroperoxides from the products of aerial oxidation of the hydrocarbons has been claimed (Union Oil Co., U.S.P. 2,430,864, 2,430,865) but no reactions of these hydroperoxides have been described. It has recently been found (Criegee and Dietrich, *Annalen*, 1948, **560**, 135) that 1-methyl- and 1-ethyl-*cyclo*hexyl hydroperoxides can be characterised by their crystalline *p*-nitrobenzoates.

Decalin 9-hydroperoxide on reduction yields *trans*-decal-9-ol (Criegee, *Ber.*, 1944, **77**, *B*, 22; Ivanov and Savinova, *Compt. rend. U.S.S.R.*, 1945, **48**, 31); the benzoate provides the same reduction product (Criegee, *loc. cit.*). It was also found by Criegee (*Ber.*, 1944, **77**, *B*, 722; *Annalen*, 1948, **560**, 127) that heating esters of decalin 9-hydroperoxide gave an isomeric hemiacetal, which on hydrolysis yielded 6-hydroxy*cyclo*decan-1-one :

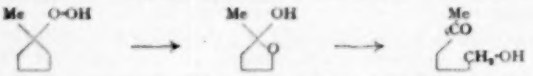
Chavanne *et al.* (for refs. see Part III, preceding paper) showed that oxidation of many alkyl*cyclo*alkanes gave ketones, alcohols, and keto-acids which very probably arose from decomposition of intermediate hydroperoxides. In the same way the many products formed from methyl*cyclo*pentane (Part III) probably arose from the hydroperoxides.

It has now been found that the decomposition products of methyl*cyclo*pentyl and methyl*cyclo*hexyl hydroperoxides can be explained by the reaction of free radicals, such as (I) and (II) which would be first formed from methyl*cyclo*pentyl hydroperoxide. Reduction of methyl*cyclo*pentyl hydroperoxide with sodium sulphite gives the expected carbinol, 1-methyl*cyclo*pentanol.

Thermal decomposition of both these hydroperoxides is slow (compared with that of phenylalkyl hydroperoxides) and gives a mixture of products, the majority ketonic. Thus

methyl*cyclo*pentyl hydroperoxide gives methyl butyl ketone, 1-methyl*cyclo*pentanol, 6-hydroxyhexan-2-one, traces of unsaturated and other ketones, and 5-ketohexanoic acid. Similarly methyl*cyclo*hexyl hydroperoxide gives mainly a mixture of methyl amyl ketone and 1-methyl*cyclo*hexanol.

Acid decomposition of methyl*cyclo*pentyl hydroperoxide provides mainly methyl butyl ketone and 6-hydroxyhexan-2-one, both derived from the same radical (II), one by gain of hydrogen and the other by gain of hydroxyl (see Part III). Alternatively the ketol may have arisen by a rearrangement similar to that of the decalin hydroperoxide esters :



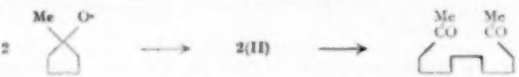
Sodium hydroxide reacts vigorously with methyl*cyclo*pentyl hydroperoxide to yield methyl butyl ketone, 1-methyl*cyclo*pentanol, and acid decomposition products including pyruvic acid. Methyl*cyclo*hexyl hydroperoxide similarly yielded mainly a mixture of methyl amyl ketone and an alcohol (presumably 1-methyl*cyclo*hexanol).

Sodium carbonate brings about a much slower decomposition of methyl*cyclo*pentyl hydroperoxide : the products again include methyl butyl ketone, but the main alcoholic constituent is 6-hydroxyhexan-2-one.

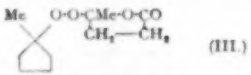
When methyl*cyclo*pentyl hydroperoxide is heated with butyraldehyde a somewhat complex reaction appears to take place. Some of the aldehyde is converted into acid but part probably condenses with the hydroperoxide. An attempt to distil the products led to rapid decomposition in which butyric acid and ketonic products were formed.

Acetone and methyl*cyclo*pentyl hydroperoxide condense in the presence of mineral acid to yield the expected 2 : 2-di-(1-methyl*cyclo*pentylperoxido)propane, which on pyrolysis gives

formaldehyde, methyl butyl ketone, and dodecane-2 : 11-dione. The diketone must have arisen through combination of two radicals formed by rearrangement :



Condensation also occurs with lævulic acid; the products probably consist mainly of the lactone (III).



(III.)

Experimental.

(M. p.s are uncorr. Elementary analyses are by Drs. Weiler and Strauss. Identities of known compounds were confirmed by mixed m. p. determinations.)

*Methyl*cyclo*pentyl and Methyl*cyclo*hexyl 1-Hydroperoxides.*—These were isolated from the products of oxidation of the corresponding *cyclo*alkanes (see Part III).

Reduction.—Methyl*cyclo*pentyl hydroperoxide (2·5 g.) and sodium sulphite (6 g.) in water (25 c.c.) were heated on the water-bath and stirred for 1½ hours. On working up of the product in the normal way, a viscous syrup (1·6 g.) was obtained, having b. p. *ca.* 135° and m. p. 35—36°, undepressed on admixture with 1-methyl*cyclo*pentanol prepared from methylmagnesium iodide and *cyclo*pentanone.

Thermal Decomposition.—(*a*) Methyl*cyclo*pentyl hydroperoxide (15 g.) was heated under reflux until the peroxide had decomposed (10 hours; after 6 hours the peroxide content was *ca.* 5%). The liquid was then distilled to give fractions (i) (1·5 g.) b. p. 90—120°, (ii) (8·3 g.) b. p. 120—130°, (iii) (1·4 g.) b. p. 130—162°, (iv) (0·5 g.) b. p. 110—135°/25 mm., (v) (0·8 g.) b. p. 135—160°/25 mm., and a residue (1·5 g.).

The main product (fraction ii) contained some methyl butyl ketone (2 : 4-dinitrophenylhydrazone, m. p. 109—110°, undepressed on admixture with a synthetic specimen), but consisted mainly of 1-methyl*cyclo*pentanol (phenylurethane, m. p. 88—89°) and 6-hydroxyhexan-2-one, which yielded a *phenylurethane*, m. p. 66—67°, much less soluble in light petroleum (Found : C, 65·9, 66·9; H, 7·4, 7·5; N, 6·4, 6·0. $C_{13}H_{17}O_3N$ requires C, 66·4; H, 7·2; N, 6·0%). Treatment of the second phenylurethane

with 2 : 4-dinitrophenylhydrazine hydrochloride yielded a 2 : 4-dinitrophenylhydrazone, m. p. 120—121·5° (from methanol).

For comparison 6-hydroxyhexan-2-one was synthesised by Lipp's method (*Ber.*, 1885, **18**, 3275; *Annalen*, 1896, **289**, 182 : cf. Colman and Perkin, *J.*, 1889, **55**, 354); it had b. p. 150—154°. It yielded the expected phenylurethane, m. p. 66—67·5°, identical with that recorded above, and this gave a 2 : 4-*dinitrophenylhydrazone*, m. p. 120—121·5° (Found : C, 55·0; H, 5·3; N, 17·0; $C_{12}H_{14}O_5N_4$ requires C, 54·9; H, 5·3; N, 16·9%), also identical with the compound described above. The ketol provided a 2 : 4-*dinitrophenylhydrazone*, m. p. 96—97° (Found : N, 19·35; $C_{12}H_{16}O_5N_4$ requires N, 19·6%).

Fraction (iii) yielded two 2 : 4-dinitrophenylhydrazones in small quantity only : (*a*) m. p. *ca.* 230°, probably the derivative of a dicarbonyl compound, and (*b*) m. p. 141—144°, shown by its ultra-violet absorption spectrum to be an $\alpha\beta$-unsaturated carbonyl derivative, probably produced by oxidation of 1-methylcyclopentene, itself obtained by dehydration of the tertiary alcohol. This fraction also contained some acid.

Fraction (v) afforded *p*-bromophenacyl 5-ketohexanoate, m. p. 90—91°.

Fraction (i) was mainly ketonic and formed a 2 : 4-dinitrophenylhydrazone, m. p. 115·5—116·5°, *i.e.*, higher than that for the corresponding derivative of methyl butyl ketone, but was not depressed on admixture. However, on analysis it appeared to be a derivative of this ketone (Found : C, 51·1; H, 5·5; N, 20·4. Calc. for $C_{13}H_{18}O_4N_4$: C, 51·4; H, 5·7; N, 20·0%). The 2 : 4-dinitrophenylhydrazones of methyl butyl ketone and methyl ethyl ketone do not depress the m. p. of one another.

(*b*) Methylcyclohexyl hydroperoxide (9·5 g.) was heated at *ca.* 140° for 3 hours, thereby completely decomposing; after 1½ hours only about 1% remained unchanged. Distillation provided fractions, b. p. 100—125° (0·8 g.) and 125—140° (5·5 g.), and a residue (1·5 g.). Both fractions appeared to be mixtures of ketones and alcohols (examination with hydroxylamine hydrochloride and methylmagnesium iodide). Both yielded a 2 : 4-dinitrophenylhydrazone, which after repeated recrystallisation melted at 85—87°, not depressed on admixture with methyl *n*-amyl ketone 2 : 4-dinitrophenylhydrazone. The semicarbazone had m. p. 120—121°, also unaltered on admixture with methyl *n*-amyl ketone semicarbazone. No phenylurethane could be isolated, but synthetic 1-methylcyclohexanol also gave no phenylurethane : the alcohol from the thermal decomposition, however, had an infra-red spectrum similar to that of the synthetic material.

Mineral Acid.—(*a*) Methylcyclopentyl hydroperoxide (15 g.) and sulphuric acid (10%; 50 c.c.) were heated at 90—100° for 2 hours. The product was extracted with ether and worked up in the normal way. Distillation gave fractions (i) (0·5 g.) b. p. 60—90°, (ii) (1·5 g.) b. p. 90—128°, (ii) (1·8 g.) b. p. 128—135°, (iv) (1·4 g.) b. p. 135—150°, (v) (1·2 g.) b. p. 120—160°/16 mm., (vi) (1·0 g.) b. p. 160—200°/16 mm., and a residue (2·5 g.). Fraction (i) consisted mainly of 1-methylcyclopentene (absorption of bromine in carbon tetrachloride). Fraction (ii) yielded methyl butyl ketone 2 : 4-dinitrophenylhydrazone, m. p. 112—113°. Fraction (iii) contained mainly methyl butyl ketone (2 : 4-dinitrophenylhydrazone) and 6-hydroxyhexan-2-one (phenylurethane, m. p. 67—68°). Fractions (iv) and (v) also contained mainly these two products. Fraction (vi) yielded a small quantity of an unidentified 2 : 4-dinitrophenylhydrazone, m. p. 160—162°. The aqueous layer, after neutralisation, was evaporated to dryness and re-extracted with ether. This gave a further quantity (*ca.* 1 g.) of 6-hydroxyhexan-2-one.

(*b*) Methylcyclohexyl hydroperoxide (10 g.) and sulphuric acid (20%; 25 c.c.) were heated together on the water-bath, until the peroxide had decomposed (14 hours). Ether-extraction yielded only 5 g. of material, mainly methyl *n*-amyl ketone (2 : 4-dinitrophenylhydrazone, m. p. 91—92°; semicarbazone, m. p. 120—121°). The minor products were not further studied.

Sodium Hydroxide.—(*a*) To sodium hydroxide (12 g.) in water (50 c.c.) methylcyclopentyl hydroperoxide (15 g.) was added slowly with shaking. The solid sodium salt of the hydroperoxide was first formed, but on slight warming an exothermic reaction ensued resulting in the formation of two layers. The mixture was warmed for a further 1½ hours. Ether-extraction yielded the neutral product (*A*); the aqueous layer on acidification and re-extraction provided acid material (*B*). On distillation (*A*) provided fractions (i) (5·8 g.), b. p. 135—140°, (ii) (2·4 g.) b. p. 140—143°, and (iii) (0·4 g.) b. p. 143—160° (residue, 0·7 g.). Fractions (i) and (ii) contained mainly 1-methylcyclopentanol (phenylurethane, m. p. and mixed m. p. 88—89°) with 15—20% of methyl butyl ketone (2 : 4-dinitrophenylhydrazone, m. p. 108—109°; semicarbazone, m. p. 119—121°). The acids (*B*) (*ca.* 1 g.) included pyruvic acid (*p*-bromophenacyl ester, m. p. and mixed m. p. 114—115°).

(*b*) Sodium hydroxide (3·1 g.), water (30 c.c.), and methylcyclohexyl hydroperoxide (10 g.) were heated at 110—120°, 10 hours being necessary for complete destruction of the peroxide. As in (*a*) a neutral (*A*) and an acid product (*B*) were produced. Product (*A*) distilled entirely at 145—155° (6·1 g.) and analysis showed it to contain ketone *ca.* 15% and alcohol *ca.* 85%. It yielded methyl *n*-amyl ketone 2 : 4-dinitrophenylhydrazone, m. p. 91—92°. The alcohol was presumably 1-methylcyclohexanol. The acids (*B*) (1·2 g.) provided a small quantity of an unidentified *p*-bromophenacyl ester, m. p. 103—104° (from methanol).

Sodium Carbonate.—Methylcyclopentyl hydroperoxide (9·5 g.) and sodium carbonate (8·7 g.) in water (30 c.c.) were heated on the water-bath for *ca.* 16 hours. As peroxide was then still present, a further quantity of carbonate (8·7 g.) was added and the mixture heated under reflux for a further 8 hours. Although traces of peroxide still remained, the product was worked up as above. The products consisted of a mixture of methyl butyl ketone (2 : 4-dinitrophenylhydrazone) and 6-hydroxyhexan-2-one (phenylurethane).

Butyraldehyde.—Methylcyclopentyl hydroperoxide (12 g.), mixed with *n*-butyraldehyde (10 g.), became warm. After the mixture had been heated on the water-bath for 2 hours, the peroxide content had decreased by 35%. Titration indicated the presence of butyric acid (2·9 g.). After removal of the

unchanged hydroperoxide, aldehyde, and most of the butyric acid by distillation under reduced pressure, increase of the bath-temp. caused rapid decomposition of the residue. This was probably due to the initial production of a hydroxy-peroxide followed by its decomposition in the presence of butyric acid at 120°.

Acetone.—Acetone (30 g.), concentrated hydrochloric acid (15 c.c.), and methyl*cyclo*pentyl hydroperoxide (20 g.) were shaken at *ca.* 0° for ½ hour and poured into water. The product was extracted with light petroleum, and the extract dried, evaporated, and distilled. The distillate (15·5 g.) was uniform pure 2 : 2-*di*-(1-*methyl*cyclo*pentylperoxide*)*propane*, b. p. 82—87°/0·15 mm., n_D^{25} 1·4565 (Found: C, 66·3; H, 10·5%; peroxide equiv., 135. $C_{13}H_{24}O_4$ requires C, 66·17; H, 10·3%; peroxide equiv., 136).

The product (18 g.) was slowly dropped through a heated tube (*ca.* 200°) into a cooled receiver. Part of the condensate was distilled to give fractions: (i) (trace) b. p. 34—55°; (ii) (1·6 g.) b. p. 55—110°; (iii) (1·5 g.), b. p. 42—73°/15 mm.; (iv) (2·0 g.) b. p. 73—110/15 mm.; (v) (0·5 g.) b. p. 110—140°/15 mm.; residue (1·0 g.). The compositions of these were: (i) mainly ether, with a little formaldehyde (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 164°; (ii) methyl butyl ketone (2 : 4-dinitrophenylhydrazone), contaminated by another carbonyl compound; (iii) mainly carbonyl compounds (not resolved); fractions (iv) and (v) crystallised when kept; after recrystallisation from light petroleum the solid dodecane-2 : 11-dione had m. p. 67·5—68·5° (see Part V).

Lævulic Acid.—(*a*) Methyl*cyclo*pentyl hydroperoxide (30 g.), lævulic acid (30 g.), and concentrated hydrochloric acid (15 g.) were shaken at 0° for ½ hour, then poured into water. The lower organic layer was extracted with light petroleum, the extract was washed with water and dried, and the lower-boiling materials removed at the water-pump. The residue was distilled, to give fractions: (i) (1·5 g.) b. p. 30—52° (mainly 45—50°)/0·2 mm.; (ii) (3·5 g.) b. p. 52—70°/0·15 mm.; (iii) (4·2 g.) b. p. 70—82°/0·15 mm.; (iv) (5·7 g.) b. p. 82—83°/0·08 mm.; and a residue (1·2 g.). Fractions (i) and (ii) were mainly unchanged hydroperoxide. Fractions (iii) and (iv) gave the following analytical figures:

	Acid equiv.	Ester equiv.	Peroxide equiv.	% Active hydrogen.	Mol. wt. (cryoscopic).
Fraction (iii)	7305	608	198	0·11	114 (?)
Fraction (iv)	2035	230	450 •	0·20	223
$C_{14}H_{24}O_4$ (III)	—	214	214	nil	214

• Variable, depending on the time of heating with KI–AcOH, owing to slow liberation of iodine.

The variation of the ester equivs. and peroxide equivs. between fractions (iii) and (iv) show the presence of two different compounds, but their constitutions appear uncertain from the above data. The figures, however, appear definitely to exclude the acid derived from (III), which would require an acid equiv. of 232 and an active hydrogen content of 0·86%.

Thanks are offered to Mr. A. R. Philpotts for infra-red examination of products containing methyl*cyclo*hexanol.

The Distillers Company Limited, Research and Development Department, Great Burgh, Epsom. [*Received, May 18th*, 1950.]

---

542. *Reactions of Organic Peroxides. Part V. Reaction of Ferrous Sulphate with Methylcyclopentyl and Methylcyclohexyl Hydroperoxides.*

By E. G. E. Hawkins and D. P. Young.

Reaction of methyl*cyclo*pentyl hydroperoxide with ferrous sulphate solution gives mainly dodecane-2 : 11-dione. Similarly methyl*cyclo*hexyl hydroperoxide forms tetradecane-2 : 13-dione, although in poorer yield. Catalytic aerial oxidation of the C_{11} diketone affords suberic acid and keto-acids.

The reaction with ferrous sulphate generally leads to decomposition of hydroperoxides with an ease which depends on the structure of the latter. Although decomposition of secondary hydroperoxides by this means may well be catalytic, yielding the corresponding ketone by loss of water (Hartmann and Seiberth, *Helv. Chim. Acta*, 1932, **15**, 1390; Hock and Lang, *Ber.*, 1942, **75**, *B*, 1051; 1943, **76**, *B*, 169, 1130), the reaction with tertiary hydroperoxides appear to be more complex. With the tertiary hydroperoxides derived from the *sec.*-alkylbenzenes, a mixture of alcohol and ketone is normally formed (see Part II), and a stoicheiometric quantity of ferrous sulphate appears to be consumed; ferric compounds are produced.

$$Ar\text{-}CR_2\text{-}O\text{-}OH \xrightarrow{FeSO_4} Ar\text{-}CR_2\text{-}OH + Ar\text{-}COR + R^-$$

When a ferrous sulphate solution is shaken with 1-methyl*cyclo*pentyl hydroperoxide an exothermic reaction ensues, with formation of a brown, insoluble ferric compound, dodecane-

2 : 11-dione (up to 60%), methyl butyl ketone, 3-methyl*cyclo*pentanol (probably derived from a small proportion of the 3-hydroperoxide present in the 1-hydroperoxide), and unidentified minor products. The diketone was unequivocally identified (see Experimental section) and its properties accord with those recorded by Bowden, Heilbron, Jones, Sargent, and Sondheimer (*J.*, 1947, 1579), and by Cason and Prout (*J. Amer. Chem. Soc.*, 1944, **66**, 46).

The reaction of methyl*cyclo*pentyl hydroperoxide evidently involves the formation and dimerisation of the free radical $Me{\cdot}CO{\cdot}[CH_2]_4{\cdot}$:

Ferrous lactate, dissolved in potassium citrate solution, also converted the hydroperoxide into diketone, whereas ferrous chloride gave mainly the ketone–carbinol mixture.

Unsuccessful attempts were made to improve the yield of diketone. The presence of sulphuric acid at least equivalent to the basic ferric salt formed improved the yield slightly, and was helpful in that the inorganic precipitate was avoided. Addition of a mutual solvent (methanol or ethanol) also improved the yield, but other organic solvents reduced it, probably because of their reactivity with free radicals. The reaction could be carried out with a fairly crude hydroperoxide, but the product from methyl*cyclo*pentane (Part III) containing a large proportion of unchanged hydrocarbon and by-products gave a poor yield. The best yields were obtained by slow addition of the hydroperoxide to the agitated ferrous salt. Temperature had little effect, except that strong cooling (−10°) inhibited the reaction; the optimum temperature appeared to be about that of the room. A fairly wide range of concentration of reactants could be employed, although at high concentrations the yield decreased. Even under a combination of the most favourable conditions, however, the yield of diketone fluctuated between 45 and 59%; probably a factor of the variation was the purity of the hydroperoxide used.

A similar reaction with ferrous sulphate takes place with 1-methyl*cyclo*hexyl hydroperoxide, but the yield of tetradecane-2 : 13-dione (Work, *J.*, 1940, 1318) is only *ca.* 12%. Catalytic oxidation of dodecane-2 : 11-dione with oxygen gave suberic acid and a keto-acid, presumably 9-ketodecanoic acid • although the latter and its derivatives could not be obtained pure.

Experimental.

M. p.s are uncorr. Elementary analyses are by Drs. Weiler and Strauss.

Reaction of 1-*Methyl*cyclo*pentyl Hydroperoxide with Ferrous Sulphate.*—(*a*) The hydroperoxide (5 g.) and ferrous sulphate heptahydrate (12 g.) in water (20 c.c.) were shaken together; the mixture became warm. Extraction with ether followed by distillation of the extract gave fractions (i) b. p. 120—180° (1·3 g.) and (ii) 180—270° (mainly 250—270°) (2·3 g.) (residue, 0·2 g.). Fraction (i) consisted mainly of a mixture of ketones (*ca.* 55%) and alcohols (*ca.* 40%) and gave the same derivatives as in (*b*) below. Fraction (ii) solidified in the receiver. Recrystallisation from ether or benzene–light petroleum gave dodecane-2 : 11-dione, m. p. 67·5—68·5° (Found: C, 72·5; H, 11·25. Calc. for $C_{12}H_{22}O_2$: C, 72·7; H, 11·1%).

(*b*) Two experiments were carried out, in each of which the hydroperoxide (50 g.; 95% pure) was added during 1¼ hours to a vigorously stirred solution of crystallised ferrous sulphate (150 g.) in 10% (w/v) sulphuric acid (350 g.), the mixture being cooled to 20°. The organic material was extracted with ether, washed, and dried; the combined products of the two experiments were freed from solvent and distilled under reduced pressure to give low-boiling material, b. p. <140°/20 mm. (60 g.), and diketone, b. p. 146°/20 mm. (32 g.; 39%, calc. on pure hydroperoxide). The first fraction was redistilled at atmospheric pressure through a Vigreux column (3 plates). This provided some ether and material, b. p. 71° (2·3 g.) and 87—88° (2·5 g.) (probably hydrocarbons), followed by a series of fractions, b. p. 128—157° (30·9 g.), without any well-marked plateaux. A small residue consisted of diketone. The distillates were mixtures of C_6 alcohols and ketones. The lowest-boiling fractions yielded methyl butyl ketone 2 : 4-dinitrophenylhydrazone, m. p. 108°; the highest-boiling material gave the same dinitrophenylhydrazone, m. p. 107°, and an orange-yellow dinitrophenylhydrazone, m. p. 126—129° (Found: C, 52·2; H, 5·1; N, 18·0. Calc. for $C_{18}H_{18}O_4N_4$: C, 51·6; H, 5·0; N, 20·0%), probably of a cyclic C_6 ketone. The higher fractions also yielded 3-methyl*cyclo*pentyl phenylurethane, m. p. 76—78°, and 1-*naphthylurethane*, m. p. 97—98° (Found: C, 76·0; H, 6·9; N, 5·15. $C_{11}H_{13}O_2N$ requires C, 76·0; H, 7·1; N, 5·2%), identical (mixed m. p.s) with authentic samples (see below); m. p.s were strongly depressed by admixture with the corresponding derivatives of 1-methyl- and 2-methyl-*cyclo*pentanol.

(*c*) The hydroperoxide (10 g.; 87% pure), dissolved in ethanol (10 c.c.), was added to a solution of ferrous sulphate (30 g.) in 10% w/v sulphuric acid (70 c.c.) and ethanol (40 c.c.). The diketone was extracted with ether and distilled, the yield being 4·4 g. (59%, calc. on the pure hydroperoxide).

• Geneva numbering.

(*d*) Rapid mixing depressed the yield, whilst addition of the ferrous salt solution to the hydroperoxide led only to one quarter of the normal yield of diketone.

Structure of the Diketone.—The product, m. p. 67·5—68·5°, contained no active hydrogen. Besides the elementary analysis given above, it had a ketone equiv. (by hydroxylamine titration) of 101, and a mol. wt. (cryoscopic in benzene) of 204 (Calc. for $C_{12}H_{22}O_2$: ketone equiv., 99; *M*, 198). It gave a strong iodoform reaction, and yielded a 2 : 4-dinitrophenylhydrazone, m. p. 181·5—182°, and a *dioxime*, m. p. 124° (Found: N, 11·8. $C_{12}H_{24}O_2N_2$ requires N, 12·3%); both derivatives were difficult to purify.

Dodecane-2 : 11-dione has been reported as having m. p. 67° (Bowden *et al.*, *loc. cit.*) and 67·4—67·8° (Cason and Prout, *loc. cit.*). The identity of the product was confirmed by the following reactions:

(i) *Hypobromite oxidation.* Sodium hydroxide (33 g.) was dissolved in water (280 c.c.), and the solution cooled; bromine (48 g.) was added slowly with stirring, the temperature being kept at 0—10°. Finely powdered diketone (10 g.) was added, and stirring continued for a further 2 hours at the same temperature and overnight at room temperature. The bromoform and carbon tetrabromide were removed in steam, and unchanged diketone (0·4 g.) extracted with ether. Acidification followed by ether-extraction and evaporation gave a product (8·1 g.) which solidified on storage. Recrystallisation from ether gave sebacic acid, m. p. 130—131° (Found: acid equiv. 100·7. Calc. for $C_{10}H_{18}O_4$: acid equiv., 101).

(ii) *Wolff–Kishner reduction.* The diketones (8·5 g.), potassium hydroxide (10 g.), ethylene glycol (40 c.c.), and hydrazine hydrate (90—95%; 8 c.c.) were heated together under reflux for 1½ hours, and then allowed to evaporate until the liquid temperature reached 180°. Refluxing was then continued for 4 hours. The distillate and residue were combined and extracted with ether. The extract yielded a liquid, b. p. *ca.* 200°, which after being heated over sodium, was redistilled to give a distillate (3·0 g.), b. p. 206—208°, n_D^{20} 1·4209. Infra-red examination, carried out by Mr. A. R. Philpotts, showed this to be almost entirely *n*-dodecane.

(iii) *Grignard reaction.* To the Grignard reagent [from methyl iodide (12 g.) and magnesium (2 g.) in ether (150 c.c.)] was added the diketone (6 g.) in ether; a solid complex settled out. On working-up of the material in the usual way, the product consisted of a thick syrup which was crystallised from ether–light petroleum. Distillation of the sticky product gave 2 : 11-*dimethyldodecane*-2 : 11-*diol* which, crystallised from ether–light petroleum, had m. p. 57—58·5° (Found: C, 73·25; H, 12·8; active H, 0·91%. $C_{14}H_{30}O_2$ requires C, 73·0; H, 13·0; active H, 0·87%). Interaction of diethyl sebacate with methylmagnesium iodide gave the same alcohol, m. p. 57—58·5°.

(iv) *Hydrogenation.* The diketone (5 g.) in dioxan (150 c.c.) was hydrogenated at room temperature and pressure over Raney nickel. Absorption was slow, but slightly more than the calculated quantity of hydrogen was taken up in 24 hours, and the product on distillation yielded dodecane-2 : 11-diol (4·1 g.), b. p. 165—170°/14 mm.; this solidified, and after recrystallisation from aqueous alcohol and then light petroleum had m. p. 54° (Found: C, 69·9; H, 12·9. Calc. for $C_{12}H_{26}O_2$: C, 71·4; H, 13·0%). Bowden *et al.* record m. p. 54—55° for this diol.

(v) *Synthesis.* An ethereal solution of methylmagnesium bromide (1 mol.) was converted into dimethylcadmium by addition of anhydrous cadmium chloride (92 g., 1 equiv.), the reaction being completed by refluxing the mixture for several hours under nitrogen. Sebacoyl chloride (96 g., 0·4 mol.) was added slowly with cooling, and the solution finally heated under reflux for 5 hours and decomposed with water and dilute hydrochloric acid. The washed ethereal layer, after removal of the solvent, left solid dodecane-2 : 11-dione, m. p. 68°, not depressed by the compound obtained from methylcyclopentyl hydroperoxide. It gave a 2 : 4-dinitrophenylhydrazone, m. p. 182°, identical with that obtained previously.

Effect of Various Conditions on the Ferrous Sulphate Reaction.—The results obtained by carrying out the reaction under a variety of conditions are shown in the Table.

Replacement of the ferrous salt by cobaltous, stannous, or cuprous salts or by lead tetra-acetate or potassium permanganate gave no diketone, although some reaction occurred. The hydroperoxide did not appear to react at all with manganous or cerous salts under similar conditions.

Reaction of 1-*Methylcyclohexyl Hydroperoxide with Ferrous Sulphate.*—The hydroperoxide (20 g.) was added, with shaking, to ferrous sulphate (50 g.) in water. The peroxide did not react as readily as methylcyclopentyl hydroperoxide at room temperature, so the mixture was heated on the water-bath for 3 hours. Ether-extraction yielded a product which on distillation gave fractions: (i) b. p. 146—156° (13·7 g.); (ii) 80—130°/20 mm. (1·3 g.); (iii) above 130°/20 mm. (1·6 g.); and a residue (0·2 g.). Fraction (i) by analysis was shown to consist of ketones and alcohols. It provided impure 2 : 4-dinitrophenylhydrazones, and after several recrystallisations a small quantity of a derivative was obtained with m. p. 91—92°, undepressed on admixture with the derivative of methyl *n*-amyl ketone. The semicarbazone had m. p. 120·5—121·5°, identical with methyl *n*-amyl ketone semicarbazone. The alcoholic component of this fraction (*ca.* 50%) was not identified. Fraction (ii) was a similar mixture of ketone and alcohol. Fraction (iii) solidified in the receiver; recrystallisation yielded tetradecane-2 : 13-dione, m. p. 76—77° (Work, *loc. cit.*, found m. p. 75°) (Found: C, 73·7; H, 11·0. Calc. for $C_{14}H_{24}O_2$: C, 74·3; H, 11·5%).

Derivatives of the Methylcyclopentanols.—The following derivatives were prepared for comparison: 1-Methylcyclopentanol (Zelinsky and Namjetkin, *Ber.*, 1902, **35**, 2683) gave a *phenylurethane*, m. p. 88—89° (Found: C, 71·0; H, 7·7; N, 6·35. $C_{13}H_{17}O_2N$ requires C, 71·2; H, 7·8; N, 6·4%), and a 1-*naphthylurethane*, m. p. 84° (Found: C, 75·9; H, 7·0; N, 5·2. $C_{17}H_{19}O_2N$ requires C, 75·8; H, 7·1; N, 5·2%). 2- and 3-Methylcyclopentanol were prepared by reduction of the corresponding ketones (Chavanne, *Bull. Sci. Acad. Roy. Belg.*, 1926, [v], **12**, 105; van Rysselberge, *ibid.*, p. 171). The 2-isomer yielded a phenylurethane, m. p. 92—94° (cf. Godchot and Bedos, *Compt. rend.*, 1926, **182**, 393), and a

1-*naphthylurethane*, m. p. 116—117° (Found: C, 75·6; H, 7·0; N, 5·1. $C_{17}H_{15}O_2N$ requires C, 75·8; H, 7·1; N, 5·2%). The 3-isomer afforded a phenylurethane, m. p. 78—79° (cf. Godchot, Cauquil, and Calas, *Bull. Soc. chim.*, 1939, **6**, 1366), and a 1-naphthylurethane, m. p. 100—101° (see above).

The peroxide was added to the ferrous salt, except where otherwise stated. "Room" temp. denotes that no special temperature control was applied.

Ferrous salt.			Hydroperoxide.			Reaction conditions.		Yield of diketone, %.
Wt., g.	Solvent.		Purity, %.	Wt., g.	Solvent.	Temp.	Rate of addition.	
Ferrous sulphate ($7H_2O$).								
100	H_2O, 250 c.c.		86	29	None	Room	Slow	55
30	,, 60 c.c.		95	6·5	,,	,,	,,	55
36	,, 72 c.c.		98·4	10·8	,,	0°	2 Hr.[1]	46—48
30	,, 300 c.c.		?	10	,,	Room	1·5 Hr.	39
30	,, 40 c.c.; EtOH, 20 c.c.		89	10	EtOH, 10 c.c.	,,	Slow	42
30	,, 60 c.c.		?	10	$COMeBu^t$ 10 g.	0°	,,	35
40	,, 2 c.c.; C_6H_6, 100 c.c.		?	10	None	10—25°	,,	14
30	,, 80 c.c.		?	10	,,	Room	,,[2]	47
150	350 c.c.		95·3	50	,,	20°	,,[2]	39
30	10% H_2SO_4, 70 c.c.; EtOH, 40 c.c.		93·2	10	EtOH, 10 c.c.	−10° rising	5 Sec.	13
30	,, ,,		87	10	,,	<10°	Slow	48
30	,, ,,		89	10	,,	20 → 40	,,[4]	59
30	,, ,,		89	10	,,	40	,,	46
30	,, ,,		93	10	,,	80	,,	41
30	,, ,,		93·2	10	,,	15 → 60	5 Sec.	36
30	,, ,,		93·2	10	,,	15 → 45	30 Sec.	31
30	,, ,,		93	10	,,	10	Slow[5]	13
60	6% H_2SO_4, 120 c.c.; EtOH, 50 c.c.		95—98	10	EtOH, 20 c.c.	10	0·5 Hr.	24
30	20% H_2SO_4, 35 c.c.; EtOH, 20 c.c.		95—98	10	EtOH, 10 c.c.	10	Slow	15
30	10% H_2SO_4, 70 c.c.; MeOH, 40 c.c.		89	10	MeOH, 10 c.c.	20 → 40	,,	50
30	10% H_2SO_4, 70 c.c.; $COMe_2$, 40 c.c.		89	10	$COMe_2$, 10 c.c.	20 → 40	,,	28
30	10% H_2SO_4, 70 c.c.; dioxan, 40 c.c.		95—98	10	Dioxan, 10 c.c.	10	,,	38
30	H_2O, 100 c.c.		98·6	10	10% NaOH, 35 c.c.	0—5	,,	34
Ferrous chloride ($4H_2O$).								
15	H_2O, 100 c.c.		87·2	10	None	20 → 40	5 Mins.	9
Ferrous lactate.								
31	H_2O, 100 c.c.; K citrate, 100 g.		?	10	,,	0	0·5 Hr.	32

[1] Under N_2. [2] Reaction mixture kept just acid during reaction with H_2SO_4. [3] See (*b*) on p. 2805. [4] See (*c*) on p. 2805. [5] $FeSO_4$ added to peroxide.

Oxidation of Dodecane-2 : 11-dione.—This work was interrupted before completion, but the following experiment illustrates the salient features of the reaction.

The apparatus consisted of a closed system comprising a flask with "recycle" stirrer, oxygen inlet, a reflux condenser leading to the gas outlet with a sodium hydroxide trap, and a device for sampling without disturbing the gas flow. The whole was immersed in a thermostatically-controlled electrically-heated oil-bath. The gas absorption was measured by means of inlet and outlet wet gas meters.

A solution of dodecane-2 : 11-dione (50 g.) in glacial acetic acid (100 c.c.) containing as catalyst manganese acetate tetrahydrate (0·1 g.), was agitated at 90°, in the above apparatus, in a slow stream of oxygen. After 3½ hours the temperature was raised to 100° to maintain the rate of absorption and after 7 hours a further addition of catalyst (0·1 g.) was made. Oxidation was discontinued after 19½ hours, 17·9 l. of oxygen having been absorbed and 0·25 mol. of carbon dioxide having collected in the exit trap. During the reaction the acidity of the solution increased, whilst the ketone content decreased by over 80%. Acetic acid was removed from the oxidate at 20 mm. pressure, and the residue was esterified with methanol and sulphuric acid. The crude ester (29 g.) was fractionally distilled at 2 mm., yielding a series of ill-defined fractions, b. p. 106—140°/2 mm. (21 g. in all). All these gave positive tests for a carbonyl group, but this appeared to be most highly concentrated in the highest-boiling fractions. The lowest fraction on hydrolysis yielded suberic acid, m. p. 138—140° (Found: equiv., 89. Calc. for $C_8H_{14}O_4$: equiv., 87), giving a *p*-nitrobenzyl ester, m. p. 80—81°. The recorded values are 141° and 85° respectively. The higher fractions were separately hydrolysed and examined for other dicarboxylic acids, but only suberic acid was isolated from them. Acidification of the sodium salts from the highest fractions to pH 4, however, yielded a product, which after recrystallisation from ether–light petroleum (by cooling to −10°) had m. p. 28—32° and acid equiv. 159. This acid readily gave a yellow 2 : 4-*dinitrophenylhydrazone*, m. p. 97—100° (from benzene–light petroleum), soluble in aqueous alkali to give a

deep-red solution (Found: C, 52·9; H, 5·9; N, 14·7. $C_{11}H_{10}O_2N_4$ requires C, 52·4; H, 6·1; N, 15·3%). The *p*-phenylphenacyl esters could not be recrystallised to beyond m. p. 63—66°. This keto-acid was probably impure 9-ketodecanoic acid, for which Barger, Robinson, and Smith recorded m. p. 47·5—48·5° (*p*-phenylphenacyl ester, m. p. 68—70°).

Thanks are offered to Mr. A. R. Philpotts for infra-red analyses, and to the Directors of the Distillers Co. Ltd., for permission to publish this paper.

The Distillers Company Limited, Research and Development Department, Great Burgh, Epsom. [*Received, May 18th*, 1950.]

---

543. *The Optical Resolution of* (±)-trans-9 : 10-*Dihydroxy*-9 : 10-*dihydrophenanthrene.*

By J. Booth, E. Boyland, and E. E. Turner.

trans-9 : 10-Dihydroxy-9 : 10-dihydrophenanthrene has been obtained in (+)- and (−)-forms by resolution of the diastereoisomeric di-(−)-menthoxyacetates. This completes the proof that the biologically produced diol has the *trans*-configuration.

The partial resolution of 9 : 10-dihydroxy-9 : 10-dihydrophenanthrene, announced in a recent communication (*J.*, 1950, 1188), has now been completed, so that the proof that the biologically produced diol (cf. Boyland and Wolf, *Biochem. J.*, 1950, **47**, 64) has the *trans*-configuration is fully confirmed.

The diol, obtained by reduction of phenanthraquinone with ethereal lithium aluminium hydride, was converted into the di-(−)-menthoxyacetates. Crystallisation of the diastereoisomeric mixture from ethyl alcohol gave erratic and unpredictable results, but crystallisation from light petroleum readily gave the optically pure (dextrorotatory) di-(−)-menthoxyacetate of the (−)-diol. This, on hydrolysis with methyl-alcoholic potassium hydroxide, gave the (−)-diol, but hydrogenolysis of the ester with ethereal lithium aluminium hydride was experimentally easier and gave a purer product. Although one of the characteristics of the (±)-diol is its readiness to crystallise well from solvents such as benzene, solutions of the (−)-diol in most organic solvents set to a jelly when cooled. From *iso*octane some indications of partial crystallisation were observed, but for analytical purposes purification by vacuum-sublimation proved the only satisfactory expedient.

The mother-liquors of the light petroleum crystallisations were, after considerable trouble, made to give the di-(−)-menthoxyacetate of the (+)-diol and from this ester the (+)-diol was obtained. It naturally formed jellies similar to those formed by the (−)-diol; when equal quantities of jellies containing the (+)- and (−)-diols, each in benzene, were mixed, the jellies liquefied and the benzene was filled with the voluminous mass of long needles of the (±)-diol.

Diacetylation of the active diols was accompanied by a change of sign of rotation. The main optical data are set out below. Where (see Experimental section) rotation varied with concentration, the highest figures observed are given here:

	(−)-Diol.	(+)-Diol.	Di-(−)-menthoxyacetate of (−)-diol.	Di-(−)-menthoxyacetate of (+)-diol.	Diacetate of (−)-diol.	Diacetate of (+)-diol.
$[\alpha]_{5780}^{20}$	−143°	+137°	+137°	−302°	+363°	−349°
$[\alpha]_{5461}^{20}$	−165	+155	+161	−349	+422	−403
	(chloroform solution)		(ethyl-alcoholic solution)		(acetone solution)	

The rotation of the (−)-diol was lower in acetone than in chloroform and still lower in ethyl alcohol. The polarity of the solvent thus has much less effect than in the case of *trans*-acenaphthylene glycol (Jack and Rule, *J.*, 1938, 188).

The optical rotations of the (−)-phenanthrenediol and related compounds in different solvents are shown in the following table ($[\alpha]_D^{21}$ with *c*, 0·25 for the first three compounds, $[\alpha]_{5461}^{20}$ for the acenaphthylene glycol).

	Dioxan.	Chloroform.	Ethyl alcohol.	Acetone.	Nitrobenzene.
(−)-**9** : 10-Dihydroxy-9 : 10-dihydrophenanthrene (sublimed specimen: see Experimental)	−130°	−128°	−76°	−110°	−132°
(+)-1 : 2-Dihydroxy-1 : 2-dihydroanthracene (from rabbit urine; cf. Booth and Boyland, *Biochem. J.*, 1949, **44**, 361)	+154	+150	+125	+173	+161
(+)-1 : 2-Diacetoxy-1 : 2-dihydroanthracene	+347	+345	+351	+316	+324
trans-Acenaphthylene glycol (values from Jack and Rule, *loc. cit.*)	—	+52	0	−25	−76

Experimental.

Resolution of the Di-(−)-menthoxyacetates of (±)-trans-9 : 10-*Dihydroxy*-9 : 10-*dihydrophenanthrene*.—To a solution of 6·55 g. (1 mol.) of the diol in 20 c.c. of pyridine were gradually added, with cooling, 2 mol. proportions of (−)-menthoxyacetyl chloride. The mixture was kept overnight and then poured into dilute hydrochloric acid. The precipitate was filtered off, washed, dried, and then crystallised 5 times from light petroleum (b. p. 40—60°). The *di*-(−)-*menthoxyacetate* of (−)-9 : 10-dihydroxy-9 : 10-dihydrophenanthrene was so obtained as slightly distorted hexagonal plates (1·85 g.), m. p. 110° (corr.), $[\alpha]_{5780}^{20}$ +137°, $[\alpha]_{5461}^{20}$ +161° (*c*, 0·3395 in absolute ethyl alcohol) (Found: C, 75·3; H, 8·4. $C_{34}H_{52}O_6$ requires C, 75·5; H, 8·7%). The mother-liquors from the above crystallisations, when evaporated, gave various crops of fluctuating rotation, but after elaborate fractionation from light petroleum (b. p. 40—60°) 0·9 g. of the *di*-(−)-*menthoxyacetate* of (+)-*trans*-9 : 10-dihydroxy-9 : 10-dihydrophenanthrene was isolated as long fine needles (frequently in the form of brushes), m. p. 117° (corr.), $[\alpha]_{5780}^{20}$ −302°, $[\alpha]_{5461}^{20}$ −349° (*c*, 0·4476 in absolute ethyl alcohol) (Found: C, 75·6; H, 8·9%).

In another series of resolution experiments, in which the dimenthoxyacetates derived from 4·6 g. of (±)-diol were crystallised once from ethyl alcohol and then 3 times from light petroleum (b. p. 60—80°), 1·35 g. of the pure di-(−)-menthoxyacetate of the (−)-diol was obtained, with $[\alpha]_{5780}^{20}$ +137° and $[\alpha]_{5461}^{20}$ +161° (*c*, 0·3965 in ethyl alcohol).

Crystallisation of the di-(−)-menthoxyacetates of the (±)-diol from ethyl alcohol gave erratic results, successive crystallisations giving crops having $[\alpha]_{5780}^{20}$ −73°, −74°, +24°, −25°, and −42° (in ethyl alcohol). The last crop, when crystallised, first gave a product with $[\alpha]_{5780}^{20}$ +120°, the mother-liquor rapidly depositing crystals having $[\alpha]_{5780}^{20}$ −282°. Presumably the partial racemate has, in ethyl alcohol, a solubility very similar to that of one of the two diastereoisomerides.

(−)-9 : 10-*Dihydroxy*-9 : 10-*dihydrophenanthrene*.—(*a*) A specimen (0·3 g.) of the dimenthoxyacetate having $[\alpha]_{5780}^{20}$ +137° in ethyl alcohol was dissolved in 15 c.c. of methyl-alcoholic potassium hydroxide (potassium hydroxide 10 g., water 10 c.c., and methyl alcohol 240 c.c.), and the solution boiled under reflux for 30 minutes and then poured into water. The solution, in which a very small amount of yellowish crystalline matter was suspended, was extracted 4 times with ether. The combined ethereal extracts were washed twice with dilute sodium carbonate solution and then 3 times with brine. Evaporation of the ethereal layer gave 0·1 g. of an orange-coloured solid, readily dissolving in benzene to give a solution which set to a gel on cooling. Removal of most of the benzene, followed by addition of light petroleum (b. p. 40—60°) gave the crude diol as a pale yellow solid having $[\alpha]_{5780}^{20}$ −129° and $[\alpha]_{5461}^{20}$ −148° (*c*, 0·1550 in chloroform).

(*b*) A second portion (0·3 g.) of the foregoing dimenthoxyacetate was dissolved in 50 c.c. of anhydrous ether, and 0·5 g. of lithium aluminium hydride added. The mixture was boiled under reflux for an hour, cooled, and treated with water and then with dilute sulphuric acid until two clear layers were obtained. The aqueous layer was extracted 3 times with ether, and the combined ethereal extracts were washed twice with brine, once with dilute sodium carbonate, and again with brine. Evaporation of the ethereal solution gave a jelly which became solid when ground with light petroleum (b. p. 40—60°), which removed ethylene glycol (−)-menthyl ether. The crude diol had $[\alpha]_{5780}^{20}$ −141° and $[\alpha]_{5461}^{20}$ −164° (*c*, 0·4400 in chloroform).

Reduction as under (*b*) of a different specimen of dimenthoxyacetate having $[\alpha]_{5780}^{20}$ +137° gave a crude diol, m. p. 162°, having (i) $[\alpha]_{5780}^{20}$ −143° and $[\alpha]_{5461}^{20}$ −165° (*c*, 0·2975 in chloroform), (ii) $[\alpha]_{5780}^{20}$ −81° and $[\alpha]_{5461}^{20}$ −91° (*c*, 0·2580 in absolute ethyl alcohol), and (iii) $[\alpha]_{5780}^{20}$ −119° and $[\alpha]_{5461}^{20}$ −135·5° (*c*, 0·1845 in acetone).

All attempts to crystallise the active diol from a solvent were unsuccessful owing to the formation of jellies. (A very concentrated solution in ethyl alcohol set to a mass of fine needles when the last traces of solvent were removed and a solution in boiling *iso*octane set on cooling to a jelly in which minute hair-like crystals were suspended.) The crude diol sublimed at 100—110°/10^{-3} mm. as a white micro-crystalline solid, m. p. 162° (Found: C, 79·4; H, 5·5; $C_{14}H_{12}O_2$ requires C, 79·3; H, 5·7%). It had $[\alpha]_D^{21}$ −135° (*c*, 1·0), −132° (*c*, 0·5), and −128° (*c*, 0·25) in chloroform; $[\alpha]_D^{21}$ −88° (*c*, 1·0), −78° (*c*, 0·5), and −76° (*c*, 0·25), $[\alpha]_{5780}^{20}$ −77°, and $[\alpha]_{5461}^{20}$ −90° (*c*, 0·3490) in absolute ethyl alcohol.

(+)-9 : 10-*Diacetoxy*-9 : 10-*dihydrophenanthrene*.—A solution of the crude (−)-diol in pyridine was treated with acetic anhydride and kept overnight. Addition of water and dilute hydrochloric acid precipitated the crude diacetate, which was washed with water. It crystallised from diluted ethyl alcohol in orthorhombic prisms, m. p. 121—122° (Found: C, 72·7; H, 5·6. $C_{18}H_{16}O_4$ requires C, 73·0; H, 5·4). It had $[\alpha]_{5780}^{20}$ +363° and $[\alpha]_{5461}^{20}$ +422° (*c*, 0·3510 in acetone).

(+)-9 : 10-*Dihydroxy*-9 : 10-*dihydrophenanthrene*.—A specimen of (−)-dimenthoxyacetate having $[\alpha]_{5780}^{20}$ −302° in ethyl alcohol was reduced in ethereal solution with lithium aluminium hydride, 0·18 g. of white solid crude diol, m. p. 162°, being obtained. It had $[\alpha]_{5780}^{20}$ +137° and $[\alpha]_{5461}^{20}$ +155° (*c*, 0·4830 in chloroform). It gave only jellies when attempts were made to crystallise it from solvents. After sublimation at 100—110°/10^{-3} mm., it was obtained as a white micro-crystalline solid, m. p. 158° (Found: C, 79·5; H, 6·3. $C_{14}H_{12}O_2$ requires C, 79·3; H, 5·7). The sublimed material had $[\alpha]_D^{21}$ +128° (*c*, 1·0), +122° (*c*, 0·5) in chloroform.

(−)-9 : 10-*Diacetoxy*-9 : 10-*dihydrophenanthrene* was obtained from the crude (+)-diol by acetylation in pyridine solution. After being crystallised from diluted alcohol, it had the same m. p. and crystalline form as the (+)-diacetate (Found: C, 72·9; H, 5·8%). In acetone solution (*c*, 0·2695) it had $[\alpha]_{5780}^{20}$ −349° and $[\alpha]_{5461}^{20}$ −403°.

Our best thanks are offered to Professor G. A. R. Kon, F.R.S., for his help with the micro-sublimations and micro-analyses. One of us (E. E. T.) is indebted to Imperial Chemical Industries Limited for financial

assistance. The investigation has been supported by grants to the Royal Cancer Hospital from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the U.S. Public Health Service.

CHESTER BEATTY RESEARCH INSTITUTE,
THE ROYAL CANCER HOSPITAL, LONDON, S.W.3.
BEDFORD COLLEGE (UNIVERSITY OF LONDON), LONDON, N.W.1. [*Received, June 27th*, 1950.]

---

544. *Allylbenzene Compounds. Part II.** 2 : 4 : 6-*Trimethoxyallylbenzene.*

By P. HOLMES, D. E. WHITE, and I. H. WILSON.

2 : 4 : 6-Trimethoxyallylbenzene has been obtained by the pyrolysis of 3 : 5-dimethoxyphenyl allyl ether, followed by methylation of the resultant phenol. The allyl group in 2 : 4 : 6-trimethoxyallylbenzene is unusually stable to alkali, but at 130° it rearranges to 2 : 4 : 6-trimethoxypropenylbenzene which forms 2 : 4 : 6-trimethoxybenzoic acid on oxidation.

THREE trimethoxyallylbenzenes have been reported to occur in Nature: elemicin, the identification of which as 3 : 4 : 5-trimethoxyallylbenzene by Semmler (*Ber.*, 1908, **41**, 1768, 1918) was confirmed by Mauthner's synthesis (*Annalen*, 1917, **414**, 250; cf. Hahn and Wassmuth, *Ber.*, 1934, **67**, 696), calamol, isolated by Qudrat-i-Khuda, Mukherjee, and Ghosh (*J. Indian Chem. Soc.*, 1939, **16**, 583) from the rhizome of *Acorus calamus* (variety "ghore bacha") and believed by them to be "2 : 3 : 5-, 2 : 3 : 6-, or 3 : 4 : 6- "trimethoxyallylbenzene, and 2 : 4 : 5-trimethoxyallylbenzene (Rao and Subramanian, *Current Sci.*, 1935, **3**, 552; *Chem. Abstr.*, 1935, **29**, 6585; 1934, **28**, 3523).

A fourth isomer, 2 : 4 : 6-trimethoxyallylbenzene, has now been synthesised. Allylation of 3 : 5-dimethoxyphenol and pyrolysis of the allyl ether gave a phenol, which is undoubtedly 3 : 5-dimethoxy-2-allylphenol, since no anomalous rearrangements of allyl ethers are known when both *ortho*-positions are unsubstituted (cf. Tarbell, *Organic Reactions*, 1944, **2**, 1). Methylation of the phenol with diazomethane or with methyl sulphate gave 2 : 4 : 6-trimethoxyallylbenzene.

Unlike the other known allylbenzenes, the refractive index of 2 : 4 : 6-trimethoxyallylbenzene was only slightly increased on prolonged heating of the compound with saturated alcoholic potassium hydroxide. However, on being heated with potassium hydroxide at 130° it isomerized readily to 2 : 4 : 6-trimethoxypropenylbenzene which was isolated as a crystalline solid and oxidised to 2 : 4 : 6-trimethoxybenzoic acid, identified by comparison with an authentic specimen, obtained from 2 : 4 : 6-trihydroxybenzoic acid. The latter was obtained by Will's method (*Ber.*, 1885, **18**, 1323) and methylated in two stages, diazomethane giving the intermediate methyl 2-hydroxy-4 : 6-dimethoxybenzoate from which either 2 : 4 : 6-trimethoxybenzoic acid or its methyl ester could be obtained by treatment with methyl sulphate and alkali. This method is preferable to those described in the literature (Beilstein, 4th Edn., **10**, 469).

EXPERIMENTAL.

3 : 5-*Dimethoxyphenyl Allyl Ether.*—Phloroglucinol dimethyl ether (Pratt and Robinson, *J.*, 1924, **125**, 188) (4·8 g.), allyl bromide (4·3 g.), potassium carbonate (freshly dried and sieved) (5·0 g.), and acetone (dried over potassium carbonate) (25 ml.) were refluxed for 7 hours and cooled, and water (100 ml.) added. The 3 : 5-*dimethoxyphenyl allyl ether* which separated was extracted with ether, washed with 5% sodium hydroxide solution, dried (K_2CO_3), and distilled. It formed a colourless oil, b. p. 156—162°/18 mm., b. p. 105—106°/0·4 mm. (Found: C, 68·2; H, 7·45. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%). From the alkaline washings phloroglucinol dimethyl ether (1·5 g.) was recovered.

3 : 5-*Dimethoxy-2-allylphenol.*—3 : 5-Dimethoxyphenyl allyl ether (12·7 g.) was heated in an oil-bath at 200—210° for 1 hour. Rearrangement began at about 180°; the temperature of the liquid rose more rapidly than that of the bath until it exceeded the bath-temperature, and after 25—30 minutes fell 1—2° below it again. On cooling, the product was dissolved in 5% sodium hydroxide solution, washed with ether to remove any unchanged allyl ether, acidified, and extracted with ether. After being dried (Na_2SO_4), evaporated, and distilled, the 3 : 5-*dimethoxy-2-allylphenol* (10·2 g.), b. p. 168—170°/18 mm., b. p. 120—121°/0·5 mm., solidified, and formed long colourless prisms, m. p. 42—43°, from light petroleum (b. p. 60—80°) (Found: C, 68·2; H, 7·5. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%).

2 : 4 : 6-*Trimethoxyallylbenzene.*—(a) *By diazomethane.* 3 : 5-Dimethoxy-2-allylphenol (5 g.) in methanol (20 ml.) was treated with an ethereal solution of diazomethane prepared from nitroso-

* *J.*, 1949, 436, is considered to be Part I.

methylurea (20·6 g.). After 60 hours at room temperature the solvents were evaporated; **2 : 4 : 6-*trimethoxyallylbenzene*** distilled as a colourless oil, b. p. 163—167°/22 mm., n_D^{25} 1·5377.

(b) ***With methyl sulphate.*** 3 : 5-Dimethoxy-2-allylphenol (15 g.) in methanol (30 ml.) was stirred and treated with methyl sulphate (15 g.) and excess of 20% sodium hydroxide solution for 30 minutes. After 15 minutes' boiling, and cooling, the 2 : 4 : 6-trimethoxyallylbenzene was extracted with ether, washed with water, dried (Na_2SO_4), and distilled. It (12·2 g.) had b. p. 156—158°/20 mm., b. p. 82—84°/0·07 mm., n_D^{25} 1·5388, n_D^{25} 1·5370, $n_D^{25\cdot4}$ 1·5322 (Found: C, 68·9; H, 7·7. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7%). Light absorption: Maximum, 2700—2730 A.; ε = 875.

Heating 2 : 4 : 6-trimethoxyallylbenzene (1 g.) with potassium hydroxide (1 g.), water (1·5 ml.), and alcohol (5 ml.) at the boiling point for 10 hours and recovery of the oil by addition of water and extraction with ether gave a product (0·7 g.), b. p. 157°/19 mm., n_D^{25} 1·5389, n_D^{25} 1·5370, $n_D^{25\cdot1}$ 1·5329.

Heating it (1 g.) with potassium hydroxide (2·6 g.) and alcohol (10 ml.) for 48 hours on a steam-bath gave an oil (0·7 g.), b. p. 167—168°/25 mm., n_D^{25} 1·5425. Increasing the time of heating to 75 hours did not give any further increase in the refractive index of the product.

2 : 4 : 6-*Trimethoxypropenylbenzene.*—2 : 4 : 6-Trimethoxyallylbenzene (3·9 g.) was dissolved in amyl alcohol (B.D.H. AnalaR; 30 ml.) and heated with potassium hydroxide (pellets; 10 g.) in an oil-bath at 125—140° for 22 hours. The amyl alcohol was removed by steam-distillation, and the residue cooled, whereupon 2 : 4 : 6-trimethoxypropenylbenzene crystallised (3·5 g.) and was filtered off. It formed long colourless prisms, m. p. 74—74·5°, from methanol (Found: C, 69·0; H, 7·7. $C_{12}H_{14}O_3$ requires C, 69·2; H, 7·7%). Light absorption: Maximum, 2675 A.; ε = 18,870.

2 : 4 : 6-*Trimethoxybenzoic Acid.*—(a) ***By oxidation.*** 2 : 4 : 6-Trimethoxypropenylbenzene (1·6 g.) was dissolved in acetone (75 ml.) and shaken with potassium permanganate (powdered; 3·3 g.) added in small portions during 30 minutes. The reaction was completed at the boiling point, and the acetone removed by steam-distillation. On cooling, sulphur dioxide was passed into the residue until the manganese dioxide dissolved and the acid was then extracted with ether, the ethereal solution extracted with sodium carbonate solution, and the acid precipitated by addition of dilute sulphuric acid. 2 : 4 : 6-Trimethoxybenzoic acid (0·1 g.) was filtered off and formed plates and prisms, m. p. 143° (decomp.), from aqueous methyl alcohol, alone or mixed with an authentic specimen prepared by method (b) below (Found: C, 56·45; H, 5·8. Calc. for $C_{10}H_{12}O_5$: C, 56·6; H, 5·7%).

(b) ***From 2 : 4 : 6-Trihydroxybenzoic Acid.*** 2 : 4 : 6-Trihydroxybenzoic acid (m. p. 206°, decomp.) (2·8 g.) was prepared in 55% yield by boiling phloroglucinol (3·8 g.), potassium hydrogen carbonate (15 g.), and water (30 ml.) for 10 minutes, cooling the mixture and pouring it into dilute hydrochloric acid. The product was dissolved in methanol (30 ml.) and ether (100 ml.) and treated with diazomethane from nitrosomethylurea (15 g.) at 5°, the temperature being allowed to rise to 20° during 1 hour. The excess of diazomethane was destroyed with acetic acid, the solvents were evaporated, and the methyl 2-hydroxy-4 : 6-dimethoxybenzoate (2·2 g.) was isolated as colourless needles, m. p. 105—106°, from methanol.

Treatment of methyl 2-hydroxy-4 : 6-dimethoxybenzoate (10 g.) in acetone (100 ml.), at the boiling point, with methyl sulphate (3 × 10 ml.) and 10%-potassium hydroxide solution (4 × 100 ml.), distillation of the solvents, and cooling and acidification of the residue gave 2 : 4 : 6-trimethoxybenzoic acid (7·9 g.), as colourless needles and plates (from 20% aqueous methanol), m. p. 142° (decomp.) after drying over phosphoric oxide.

If the methylation mixture was refluxed for two hours before removal of the solvents, the product was decarboxylated to phloroglucinol trimethyl ether, which crystallised on cooling, whilst cooling the reaction mixture two minutes after addition of the potassium hydroxide resulted in the separation of methyl 2 : 4 : 6-trimethoxybenzoate, which formed colourless prisms, m. p. 68—69°, from aqueous methanol and was hydrolysed to 2 : 4 : 6-trimethoxybenzoic acid when boiled for 1 hour with 5% aqueous alcoholic potassium hydroxide.

Thanks are offered to the Commonwealth Research Grant to Australian Universities for a grant, to Drs. Weiler and Strauss, Oxford, for the microanalyses, and to Miss B. J. Levien and Mr. W. Bottomley for the absorption spectra, observed with a Beckman model DU spectrophotometer.

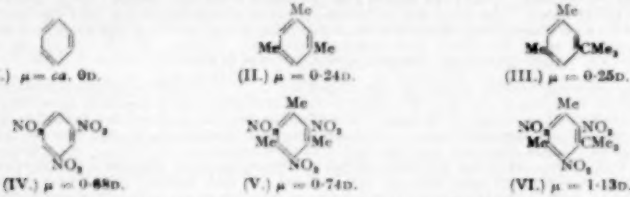
UNIVERSITY OF WESTERN AUSTRALIA. [*Received, July 3rd*, 1950.]

545. *The Ultra-violet Spectra of Certain Substituted Aromatic Nitro-compounds.*

By P. Fielding and R. J. W. Le Fèvre.

Comparison of the ultra-violet absorption spectra of trinitromesitylene and trinitro-*tert.*-butylxylene with those of mono-, di-, and tri-nitrobenzenes reveals in the first two a diminution of intensity and wave-length of the 260 mμ. (log ε, 3·9) band attributable to the $Ar{\cdot}NO_2$ system. An explanation based on the steric inhibition of resonance is in line with previous data in the literature.

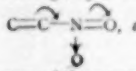
In a recent communication (*J.*, 1950, 1829) Le Fèvre and Le Fèvre compared *inter alia* the dipole moments of the hydrocarbons (I)—(III) with those of their symmetrical trinitro-derivatives (IV)—(VI). The apparent orientation polarisation of (VI) was found to exceed that of (III) by 25 c.c., while the corresponding disparities between (IV) and (I), and between (V) and (II) were



(I.) $\mu = ca.$ 0D. (II.) $\mu = 0{\cdot}24$D. (III.) $\mu = 0{\cdot}25$D.

(IV.) $\mu = 0{\cdot}68$D. (V.) $\mu = 0{\cdot}74$D. (VI.) $\mu = 1{\cdot}13$D.

both only *ca.* 10 c.c. Trinitration therefore affects polarity most in the case of *tert.*-butylxylene and causes, from (III) to (VI), a change of $\mu_{apparent}$ which is unexpectedly great (cf. Coop and Sutton, *J.*, 1938, 1269). Of the possible reasons for this, those implicit in the phrase "steric inhibition of resonance" seemed applicable, in view of the greater space requirements of CMe_3 than of Me. Scale drawings (such as Figs. 1 and 2 of *J.*, 1935, 957) show overlap between the "*X*-ray" dimensions of *tert.*-butyl and those of two vicinal nitro-groups, while when methyl replaces butyl the interference involves only the "Wirkungsradien." In (VI) therefore, of the three nitro-groups, that *para* to CMe_3 should be least prevented from polarising in the sense



and—because of this—could outweigh in the molecular resultant the vector sum of the components associated with the other two (less polarised) nitro-substituents.

Such opposition by steric factors to the assumption of planar configurations may be displayed in the ultra-violet absorption spectra of the substances concerned (Remington, *J. Amer. Chem. Soc.*, 1945, **67**, 1838, among others, has set out the qualitative explanation of the variations of wave-length and intensity to be expected between parent structures and their "hindered" derivatives; cf. also Wheland, "The Theory of Resonance," Wiley & Sons, 1944, pp. 160—162). Sherwood and Calvin (*J. Amer. Chem. Soc.*, 1942, **64**, 1350) and Remington (*loc. cit.*) had noted the weakening of the characteristic nitro-absorption band at 2500—2600 by *o*-Me, and Brown and Reagan (*ibid.*, 1947, **69**, 1032) have lately demonstrated that the effect becomes progressively greater as the volume of the *ortho*-hydrocarbon radical is increased.

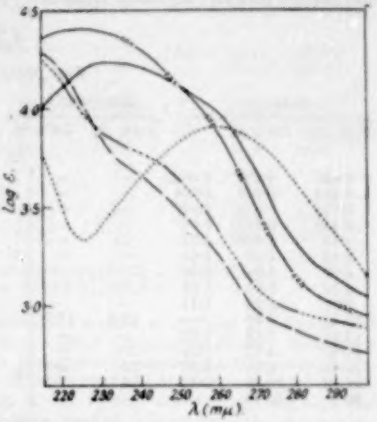
Present Work.—In view of its obvious relevance we have applied the method to structures (IV), (V), and (VI), nitro- and *m*-dinitro-benzene being included for comparison. Absorption determinations were made with the "Beckman photoelectric quartz spectrophotometer, Model DU." Our solvent has been 96% alcohol throughout (Brown and Reagan used *iso*octane).

Results are shown in the figure; details of the clear maxima read from the large-scale originals are tabulated below.

Solute.	$\lambda_{max.}$ (mμ.).	log $\varepsilon_{max.}$
Nitrobenzene	260	3·91
m-Dinitrobenzene	235	4·24
s-Trinitrobenzene	225	4·41
s-Trinitromesitylene	Below 220	Above 4·2
Trinitro-*tert.*-butylxylene	Below 220	Above 4·2

We note that our curve for nitrobenzene in ethyl alcohol agrees with that of Brown and

Reagan (*loc. cit.*; $\lambda_{max.}$ = 2520, $\varepsilon_{max.}$ = 8620, in *iso*octane). Dinitro- and trinitro-benzenes show slight " shoulders " suggestive of maxima just below 260 mμ., with intensities indicated by log ε values *ca.* 4; with the mesitylene and butylxylene derivatives the corresponding points appear to lie in the region 240—250 mμ. with log ε about 3·2, the butyl compound being the lower. The spectra of the last two substances resemble somewhat those obtained for nitromesitylene and *o*-nitro-*tert.*-butylbenzene by Brown and Reagan. Following these authors we recognise the " shoulders " in the figure as residual 260-mμ. nitro-group absorptions whose positions and intensities indicate reduction or otherwise of resonance conferring a partial double-bond character on the Ar-nitro-link. In this respect therefore mono-, di-, and trinitrobenzenes are approximately equally unaffected, while in compounds (V) and (VI) such resonance is diminished. The broad short-wave maxima of the di- and tri-nitrobenzenes may accordingly be viewed as *E*-bands, displaced towards lower frequencies.



Nitrobenzene .....
m-*Dinitrobenzene* .....
s-*Trinitrobenzene* .....
Trinitromesitylene .....
Trinitro-tert.-*butylxylene*

The spectra of the last two substances do not appear to have been much investigated. Rădulescu and Elexa (*Bul. Soc. chim. Romania*, **1935**, **17**, 69; *Chem. Abs.*, **1936**, **30**, 2111) report certain measurements in absolute alcohol and 0·2N-ethyl-alcoholic sodium ethoxide, but the abstract does not record quantitative data, and the original is not available to us. Kortüm (*Z. physikal. Chem.*, **1939**, *B*, **42**, 39) shows graphically, for nitrobenzene and *m*-dinitrobenzene in water and *s*-trinitrobenzene in 10^{-3}N-hydrochloric acid, absorptions at *ca.* 270 mμ. (log ε, 3·9), *ca.* 220 mμ. (log ε, 4·2), and below 230 mμ. (log ε, above 4·4), respectively. His results and ours, therefore, despite the change of solvent, are not very dissimilar.

We are indebted to the Commonwealth Science Fund for a research grant.

UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, May 17th*, **1950**.]

---

546. *The Systems Zinc Oxide–Phosphoric Oxide–Water and Manganous Oxide–Phosphoric Oxide–Water at Temperatures between 25° and 100°.*

By J. E. SALMON and H. TERREY.

The evidence provided by phase-diagram studies has indicated the existence of an unstable zinc phosphate, $Zn(H_2PO_4)_2.2H_3PO_4$, and an anhydrous manganous phosphate, $Mn(H_2PO_4)_2$, neither of which has been previously reported.

Apart from one point concerning zinc secondary phosphate monohydrate, $ZnHPO_4.H_2O$, the results of Eberly, Gross, and Crowell on the zinc phosphates have been confirmed, and have been extended.

In the case of the manganous phosphates, no evidence has been found to support the results of Grube and Staesche. Amadori's data for the system at 25° have been found to be correct and have been extended to cover the range up to 100°.

It has been observed that the phosphates which separate from the more dilute solutions in these two systems all have a negative temperature coefficient of solubility. A similar behaviour has been found in the system ferrous oxide–phosphoric oxide–water. The inference is drawn that this behaviour is connected with the decrease in the degree of ionisation of phosphoric acid with rise of temperature, for which evidence was indicated by earlier investigators.

THE effect of temperature variations on the two systems mentioned in the title has hitherto received only slight attention. The zinc phosphate system was examined by Eberly, Gross, and Crowell (*J. Amer. Chem. Soc.*, **1920**, **42**, 1433) at 25° and 37°. Over this comparatively short

range of temperature they found that one of the stable solid phases, namely, the tertiary zinc phosphate, $Zn_3(PO_4)_2.4H_2O$, had a negative temperature coefficient of solubility. Their results also implied that zinc secondary phosphate monohydrate showed a similar behaviour.

TABLE I.

Zinc phosphate solutions.

Solution.			Moist solid.*			Solution.			Moist solid.*		
P_2O_5, %.	ZnO, %.	*d*.	P_2O_5, %.	ZnO, %.		P_2O_5, %.	ZnO, %.	*d*.	P_2O_5, %.	ZnO, %.	
					(*a*) At 25°.						
0·435	0·231	1·002	—	—		35·5	16·6	—	35·8	19·7	
0·489	0·267	1·004	—	—		37·3	15·95	1·63	37·8	25·6	C
0·714	0·373	1·007	—	—		39·8	15·91	—	39·7	27·2	
0·935	0·484	1·01	—	—		40·6	15·75	—	40·5	20·0	
1·16	0·586	1·01	—	—		44·9	13·06	1·67	47·1	26·0	
3·13	1·52	1·04	—	—	A	49·6	9·03	—	47·7	24·4	
4·07	1·95	1·04	—	—		53·7	7·66	—	48·3	24·2	D
4·09	1·95	1·04	—	—		55·3	7·23	1·67	48·2	24·9	
8·72	4·26	1·11	—	—		57·0	7·51	1·72	52·5	17·1	
11·60	5·59	—	19·2	17·7		57·3	7·75	—	57·0	8·92	
14·92	7·28	1·23	—	—		59·1	5·25	—	60·2	12·19	
17·87	8·63	1·28	—	—		60·3	3·72	—	60·9	7·52	E
19·38	9·30	1·30	22·1	14·0	B	62·1	2·45	1·69	62·1	7·56	
21·03	10·13	1·33	24·7	17·5		63·5	1·55	1·69	—	—	
26·4	12·64	—	—	—							
					(*b*) At 37°.						
0·467	0·236	1·00	—	—		17·04	8·26	1·25	—	—	A
0·907	0·442	1·01	20·8	35·6		18·02	8·76	1·27	—	—	
0·984	0·508	1·01	—	—		18·02	8·70	1·26	28·2	29·4	
4·10	1·85	1·05	12·5	17·6	A	19·56	9·70	1·30	—	—	
7·69	3·50	1·10	—	—		21·07	10·68	1·34	—	—	B
7·77	3·49	1·09	18·3	24·8		24·13	12·27	1·39	—	—	
13·66	6·49	1·19	25·4	35·6		32·7	11·94	—	47·7	26·2	D
14·49	6·84	1·20	—	—		55·1	10·66	—	—	—	
					(*c*) At 50°.						
0·84	0·40	1·001	—	—		28·3	14·74	1·45	—	—	A
1·61	0·68	1·01	—	—		29·6	15·60	1·52	—	—	
4·93	2·01	1·05	—	—		30·0	15·97	1·52	30·0	17·1	
6·64	2·78	1·07	20·3	30·7		31·3	16·34	1·54	32·3	24·1	B
7·67	3·22	1·08	—	—		34·4	17·48	1·64	—	—	
10·58	4·62	1·12	—	—		35·3	17·49	1·62	34·1	25·1	
13·86	6·23	1·14	—	—		38·7	17·30	1·65	39·2	36·4	
17·56	8·27	1·24	21·18	19·52	A	41·3	17·73	—	—	—	
17·91	8·51	1·26	21·14	19·48		41·4	18·01	—	40·5	30·1	C
18·31	8·68	1·27	—	—		43·5	17·34	—	—	—	
22·04	10·98	1·33	—	—		45·9	15·98	—	45·0	20·2	
22·61	11·40	1·36	25·9	30·0		49·3	17·2	—	49·3	18·0	
23·56	11·90	1·37	27·1	30·2		50·9	15·36	—	51·1	15·4	
27·4	14·35	1·46	28·5	25·4		53·4	12·62	—	54·0	14·23	
27·5	14·41	1·46	—	—		56·7	11·93	—	55·4	12·48	
					(*d*) At 60°.						
3·98	1·54	1·02	—	—		26·6	13·79	1·44	—	—	A
7·93	3·20	1·08	—	—		28·6	15·37	1·49	—	—	
10·43	4·42	1·12	—	—	A	32·7	16·81	1·58	33·1	24·4	B
16·21	7·52	1·22	—	—		36·2	18·42	1·65	34·4	30·0	
23·10	11·64	1·36	—	—							
					(*e*) At 75°.						
1·56	0·58	—	—	—		25·7	13·27	—	30·3	48·0	A
7·27	2·68	—	12·8	12·9		26·3	13·78	—	—	—	
7·32	2·66	—	—	—		26·7	13·96	—	—	—	
13·57	5·71	—	—	—	A	27·2	14·25	—	31·4	49·5	
18·77	8·72	—	30·2	49·0		29·8	16·32	—	31·9	49·5	
24·42	12·33	—	30·9	49·8		31·3	17·49	—	36·7	43·4	
24·73	12·59	—	—	—		35·7	18·47	—	36·5	26·6	C
25·0	12·80	—	30·0	3·89		45·3	25·2	—	—	—	

TABLE I—*continued.*

Solution.			Moist solid.			Solution.			Moist solid.		
P_2O_5, %.	ZnO, %.	*d*.	P_2O_5, %.	ZnO, %.		P_2O_5, %.	ZnO, %.	*d*.	P_2O_5, %.	ZnO, %.	
					(*f*) At 86·3°.						
0·77	0·26	0·99	4·50	6·59		23·51	11·79	1·32	25·91	25·96	
1·52	0·50	0·99	6·46	8·90		23·84	11·99	—	26·56	25·71	
7·36	2·61	1·05	12·34	12·83		24·02	12·17	—	—	—	A
13·63	5·67	1·16	18·24	18·12	A	26·4	13·60	—	31·3	49·0	
15·43	6·66	1·19	—	—		29·1	15·65	—	32·9	42·9	
18·06	8·29	1·18	22·45	24·36		32·9	18·20	—	36·8	32·3	C
20·90	10·05	1·26	—	—		38·5	20·09	—	39·2	28·0	
22·83	11·38	1·31	26·37	28·99							
					(*g*) At 100°.						
7·37	2·52	—	—	—		21·29	10·33	—	26·5	31·3	A
13·94	5·81	—	—	—	A	21·93	10·88	—	26·9	30·5	
17·82	8·08	—	23·0	24·6							

* Solid phases: A = $Zn_3(PO_4)_2.4H_2O$. B = $ZnHPO_4.3H_2O$. C = $ZnHPO_4.H_2O$. D = $Zn(H_2PO_4)_2.2H_2O$. E = $Zn(H_2PO_4)_2.2H_2PO_4$.

By studying the corresponding manganous phosphate system at 25° and 55°, Grube and Staesche (*Z. physikal. Chem.*, 1927, **130**, 572) covered a wider temperature range. Their work indicated that all the solid phases occurring in this sytem possessed positive temperature coefficients of solubility. However, their results for the system at 25° were not in agreement with those previously published by Amadori (*Atti R. Ist. Veneto*, 1921—2, **81**, 603), and the compounds which, according to them, separated from solution differed from the manganous phosphates described by earlier workers, such as Erlenmeyer and Heinrich (*Annalen*, 1878, **190**, 191). In particular, they reported that they obtained the tertiary phosphate from dilute solution in an anhydrous form, whereas other workers have always found it to be hydrated.

The work of Travers and Perron (*Ann. Chim.*, 1924, **1**, 298) on the dissociation of zinc primary phosphate in solution and the corresponding investigation by Viard (*Compt. rend.*, 1899, **129**, 412; *Bull. Soc. chim.*, 1899, **21**, 807) of the manganous primary phosphate supplemented the evidence provided by the phase-diagram studies. [Data published by Sokolovsky and Koulagina for manganous phosphates at 100° (*J. Appl. Chem. U.S.S.R.*, 1945, **18**, 412) seem to be identical with those given by Viard.] Both primary phosphates were shown to be partly dissociated in solution [*e.g.*, $3Zn(H_2PO_4)_2 \rightleftharpoons Zn_3(PO_4)_2 + 4H_3PO_4$] and in the more dilute solutions this occurred to a greater extent at 100° than at room temperature. In the case of the zinc phosphate, this result was in accord with the decreasing solubility of the tertiary phosphate established by Eberly, Gross, and Crowell (*loc. cit.*). To reconcile the results of Viard's work on manganous phosphates with those of Grube and Staesche, however, it would be necessary to postulate that a reverse in the solubility coefficient of the phase in equilibrium with dilute solutions took place between 55° and 100°. The possibility was one to be taken into account, because a change in the solid phase apparently also occurred within this range. A secondary–tertiary phosphate was found by Viard at 100° in approximately the same range of concentration as Grube and Staesche had given for the stability of the anhydrous tertiary phosphate.

It was evident that more complete information was needed on the behaviour of both systems with variation of temperature. A study was accordingly made at several temperatures between 25° and 100° and a summary of the results is given below.

Within the chosen range of temperature, five compounds occurred as stable solid phases in the zinc phosphate system. They were: (*a*) A diacid primary phosphate, $Zn(H_2PO_4)_2.2H_3PO_4$; (*b*) a primary phosphate dihydrate, $Zn(H_2PO_4)_2.2H_2O$; (*c*) a secondary phosphate monohydrate, $ZnHPO_4.H_2O$; (*d*) a secondary phosphate trihydrate, $ZnHPO_4.3H_2O$; (*e*) a tertiary phosphate tetrahydrate, $Zn_3(PO_4)_2.4H_2O$.

All of these compounds had been described by Eberly, Gross, and Crowell, except the first. This diacid primary phosphate is an unstable compound and it has not been isolated. It was found to be stable in contact with the most concentrated solutions at 25° (Fig. 1), but would not crystallise at higher temperatures.

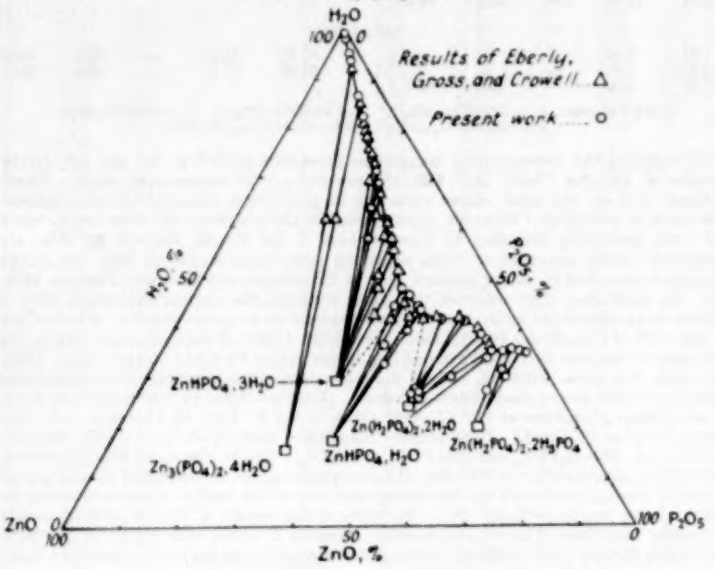
Above 37°, the primary phosphate would not crystallise but formed syrupy supersaturated solutions. Consequently, it was not possible to add to the information already published by Eberly, Gross, and Crowell.

Some light has been thrown on the conditions under which the two hydrates of zinc secondary

phosphate are stable. The monohydrate has proved to be more soluble as the temperature increases, in spite of the implication to the contrary in the work of Eberly, Gross, and Crowell. It forms a stable phase in the system at 25°, although these authors were unable to crystallise it at that temperature. Both sets of results are shown in Fig. 1, from which it can be seen that good agreement was obtained except in the range where this secondary phosphate monohydrate is the stable solid phase. Neither of the hydrates of the secondary phosphate crystallised well (they formed woolly masses of crystals) and neither was stable except in contact with its mother-liquor.

The solubility of the tertiary phosphate was found to decrease with rise of temperature up to 100°.

FIG. 1.—ZnO–P_2O_5–H_2O at 25°.



Within the same range of temperature, the manganous phosphates which were stable in contact with saturated solutions were: (*a*) A mono-acid primary phosphate, $Mn(H_2PO_4)_2,H_3PO_4$; (*b*) an anhydrous primary phosphate, $Mn(H_2PO_4)_2$; (*c*) a hydrated primary phosphate, $Mn(H_2PO_4)_2.2\frac{1}{2}H_2O$; (*d*) a secondary phosphate trihydrate, $MnHPO_4.3H_2O$; (*e*) a secondary–tertiary phosphate pentahydrate, $Mn_3(PO_4)_2.2MnHPO_4.5H_2O$.

The second of these does not seem to have been described before. It forms a stable phase in the system at 75°, but not at 50° or lower temperatures. At 75°, it is stable only in contact with its mother-liquor (Fig. 4).

All the other compounds were reported by Erlenmeyer and Heinrich or by Amadori. The mono-acid compound was shown by Amadori to crystallise from the most acid solutions at 25°. It has been established that it forms a stable phase up to 50° (Fig. 3) (also Table II, *b* and *c*). Above that temperature its field is replaced by that of the anhydrous primary phosphate.

The hydrated primary phosphate was regarded by Amadori and also by Erlenmeyer and Heinrich as being a dihydrate, whereas Grube and Staesche considered it to be a trihydrate. The results of the present work, however, suggest that, in fact, it may crystallise with $2\frac{1}{2}$ molecules of water.

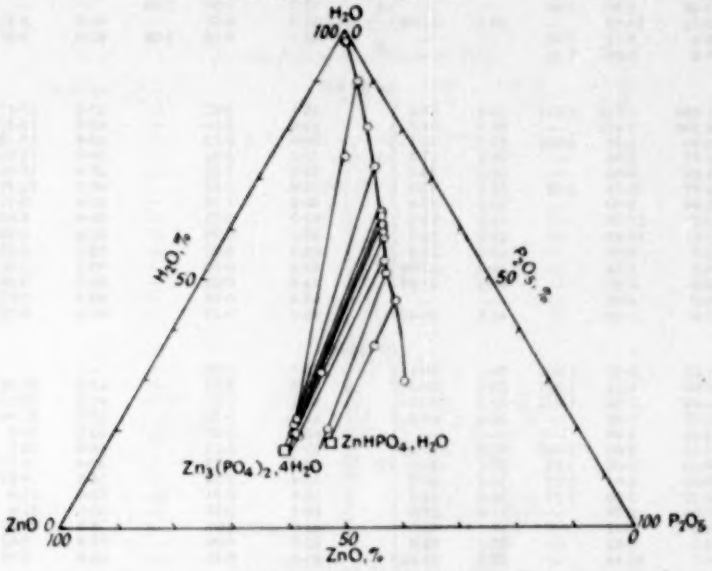
The conditions under which the secondary phosphate forms a stable phase at 25° were described by Amadori. It is stable over practically the same range of concentration at 37° but it does not appear in the system at 50° or above (Figs. 3 and 4).

The secondary–tertiary phosphate which replaced the secondary phosphate at 50° and above (Fig. 4) was the pentahydrate described by Amadori and not the tetrahydrate discovered by Erlenmeyer and Heinrich and reported also by Bassett and Bedwell (*J.*, 1933, 877). The conditions necessary for the crystallisation of this tetrahydrate have not been established.

At no temperature was the tertiary phosphate evident as a stable phase in the system, although the possibility that it possesses an extremely narrow field in the region of very dilute solutions is not precluded.

On the whole, Amadori's results for the system at 25° have been confirmed. No such agreement can be registered with any of the results of Grube and Staesche except for their solubility data at 25°, and they accord with those of Amadori.

FIG. 2.—ZnO–P_2O_5–H_2O *at* 75°.



The results now obtained for the two systems are presented in Tables I and II, respectively. Figs. 1 and 2 show the system zinc oxide–phosphoric oxide–water at 25° and 75°, respectively, and Figs. 3 and 4 the corresponding manganous oxide system at 37° and 75°.

Decrease in solubility with rise of temperature occurred among the zinc phosphates only in the tertiary compound, which separated from the more dilute solutions. The compositions of saturated solutions in equilibrium with this phosphate at different temperatures are shown in Fig. 5. This fall in solubility meant that as the temperature was increased its field on the phase diagram encroached on that of the secondary phosphate trihydrate, which gave evidence of a fairly marked increase in solubility with rise of temperature. Because the solubility of the secondary phosphate monohydrate increased but little with temperature, its field likewise encroached on that of the trihydrate. As a result the trihydrate did not appear in the system at 75° (Fig. 2).

In the manganous phosphate system a complication is introduced by the transition, at just below 50°, from the secondary phosphate to the secondary–tertiary phosphate as the stable phase in the region of more dilute solutions. The compositions of saturated solutions in this range at different temperatures are plotted in Fig. 6, from which it is apparent that the solubilty falls with rise of temperature. The compounds separating from the more concentrated solutions, on the other hand, showed an increasing solubility with rise of temperature.

It is apparent that in both systems the fall in solubility with rise of temperature is restricted to solutions containing 30% of phosphoric oxide or less, and these may for this purpose be described as "dilute" solutions. The inference is that dilute phosphoric acid solutions are less

TABLE II.

Manganous phosphate solutions.

Solution.			Moist solid.*			Solution.			Moist solid.*		
P_2O_5, %	MnO, %	*d*.	P_2O_5, %	MnO, %		P_2O_5, %	MnO, %	*d*.	P_2O_5, %	MnO, %	
(*a*) At 25°.											
0·764	0·375	1·007	—	—		49·3	1·93	1·50	48·9	24·1	B
18·44	7·83	1·26	—	—	A	57·7	1·30	1·59	—	—	
25·12	10·29	—	26·12	12·95		61·2	0·65	—	60·9	4·27	C
29·1	9·13	1·40	—	—		64·1	0·16	1·66	63·8	3·67	
37·3	5·09	1·41	—	—	B						
(*b*) At 37°.											
1·260	0·619	1·011	29·9	30·4		43·1	3·92	—	47·0	19·17	
3·206	1·475	—	26·7	26·5		48·0	2·88	—	48·6	19·37	
5·96	2·58	1·058	33·8	34·1		50·9	2·35	—	48·9	17·73	B
10·57	4·56	—	28·4	27·3	A	52·4	2·04	—	50·0	14·26	
14·26	6·05	—	28·4	26·4		56·9	1·69	—	51·4	16·02	
19·67	8·13	1·26	33·4	32·5		59·6	1·94	—	49·7	21·57	
22·66	9·50	—	31·1	27·4		60·6	1·19	—	60·8	5·12	
28·2	11·70	—	43·9	23·4		61·7	0·71	—	60·8	6·03	
29·3	10·98	—	46·6	23·7		62·1	0·78	—	62·4	5·36	
33·6	8·20	—	48·8	24·4		63·0	0·31	—	63·6	4·45	C
38·3	5·84	—	46·6	22·06	B	63·5	0·52	—	63·6	5·30	
39·0	5·39	—	47·3	21·94		64·0	0·29	—	64·0	3·36	
40·0	4·86	—	—	—		64·4	0·28	—	63·9	5·62	
41·9	4·43	—	47·1	20·46		65·0	0·25	—	64·5	3·79	
(*c*) At 50°.											
1·25	0·57	1·005	30·1	36·1		33·4	9·98	—	—	—	
2·95	1·21	1·027	30·5	38·4		33·5	9·36	—	44·8	20·86	
4·40	1·76	1·046	32·4	40·5		34·1	8·87	—	47·3	23·84	
4·73	1·85	—	39·4	48·8		41·4	5·70	—	47·0	21·04	
6·89	2·94	—	—	—		42·7	5·25	—	45·3	18·2	B
7·81	3·05	1·082	37·8	47·4		51·1	3·24	—	49·9	16·7	
9·28	3·56	1·10	36·1	45·1	D	53·5	2·73	—	52·0	9·27	
10·50	4·04	1·12	36·8	45·7		55·4	2·54	—	53·3	8·93	
20·20	7·99	1·27	36·9	44·7		56·8	2·24	—	52·0	15·9	
21·04	8·28	—	31·9	32·8		60·2	2·26	—	55·8	21·4	
24·2	9·41	—	38·1†	48·0†		61·0	2·08	—	58·0	20·60	C
25·3	9·65	—	33·1	32·0		62·8	0·99	—	62·3	6·82	
28·7	11·44	—	32·4	23·07		63·4	0·87	—	63·6	6·36	

† Solid washed and left to dry in the air before analysis.

(*d*) At 75°.											
4·29	1·46	—	—	—		46·1	6·63	—	46·1	14·47	
4·41	1·49	—	38·2	47·8		47·7	5·73	—	—	—	B
8·25	2·58	—	28·9	33·4		52·6	5·35	—	—	—	
14·29	5·16	—	38·6	48·0		57·6	3·86	—	53·3	15·94	
16·91	5·95	—	36·9	45·3		58·6	3·33	—	55·7	21·3	
21·1	7·58	—	27·1	21·2	D	59·8	2·98	—	56·5	11·4	
27·8	10·17	—	32·1	23·43		60·2	2·53	—	57·2	19·61	
30·4	11·04	—	—	—		60·9	2·21	—	59·2	12·4	E
34·5	13·02	—	—	—		61·6	2·20	—	60·1	8·15	
35·5	12·45	—	—	—		62·2	1·65	—	58·5	17·8	
35·7	12·89	—	36·0	18·38		63·6	1·58	—	62·8	4·30	
						63·9	1·70	—	58·2	19·98	
(*e*) At 85°.											
2·58	0·78	—	34·2	42·3	D	11·56	3·48	—	32·8	39·1	D
3·46	1·02	—	36·6	45·9		22·22	7·18	—	32·2	32·4	
5·92	1·82	—	33·1	40·2		27·32	9·68	—	—	—	

* Solid phases: A = $MnHPO_4.3H_2O$. B = $Mn(H_2PO_4)_2.2\frac{1}{2}H_2O$. C = $Mn(H_2PO_4)_2.H_3PO_4$.
D = $Mn_3(PO_4)_2.2MnHPO_4.5H_2O$. E = $Mn(H_2PO_4)_2$.

TABLE II—*continued.*

	Solution.		Solid.†		
No.	P_2O_5, %.	MnO, %.	P_2O_5, %.	MnO, %.	H_2O, %.
		(*f*) At boiling temperature.			
1	—	—	38·4	48·2	—
2	1·27	0·33	38·9	48·1	—
Calc. for $Mn_3(PO_4)_2.2MnHPO_4.5H_2O$			38·04	47·49	14·47
,, $Mn_3(PO_4)_2.2MnHPO_4.4H_2O$			38·98	48·66	12·36

† The solids which separated from these solutions were washed and left to dry in the air before analysis.

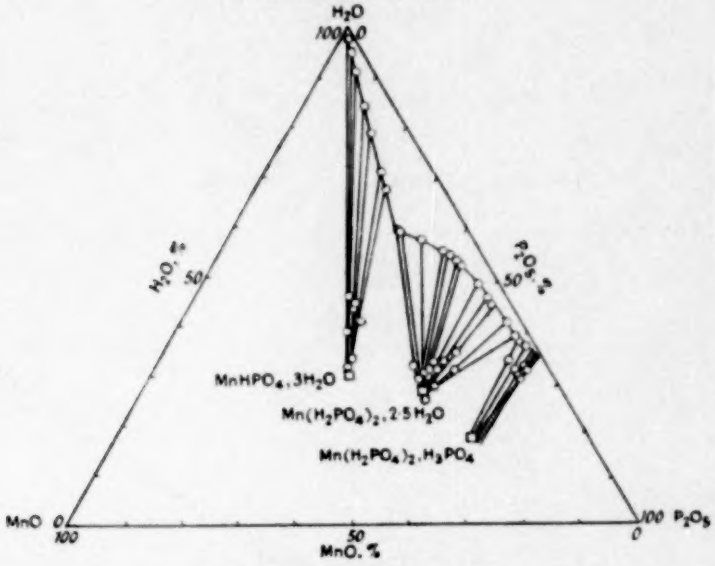
Solution 1 made from 3·50 g. of primary phosphate and 100 ml. of water.
Solution 2 made from 3·00 g. of primary phosphate and 100 ml. of water.

TABLE III.

Ferrous phosphate solutions at 25°.

Solution	P_2O_5, %	9·15	12·27	14·40	17·19
	FeO, %	4·20	5·51	7·57	7·49

FIG. 3.—MnO–P_2O_5–H_2O *at* 37°.



able to retain heavy-metal phosphates in solution as the temperature increases. Otherwise stated, as the temperature rises, the reaction

$$3M(H_2PO_4)_2 \rightleftharpoons M_3(PO_4)_2 + 4H_3PO_4$$

is displaced to the right. Now the equation may be rewritten as

$$3M^{++} + 6H_2PO_4^- \rightleftharpoons M_3(PO_4)_2 + 4H^+ + 4H_2PO_4^-$$

which implies that the reaction will go to the right if the hydrogen and phosphate ions are removed in the form of un-ionised molecules or possibly ion pairs. For such a reaction to account for the behaviour of the phosphates there must be a reduction in the degree of ionisation

of phosphoric acid as the temperature increases. It has been assumed that only the first stage of ionisation of phosphoric acid need be considered, and support for this is provided by the low value of K_1 for the acid.

FIG. 4.—MnO–P_2O_5–H_2O *at* 75.

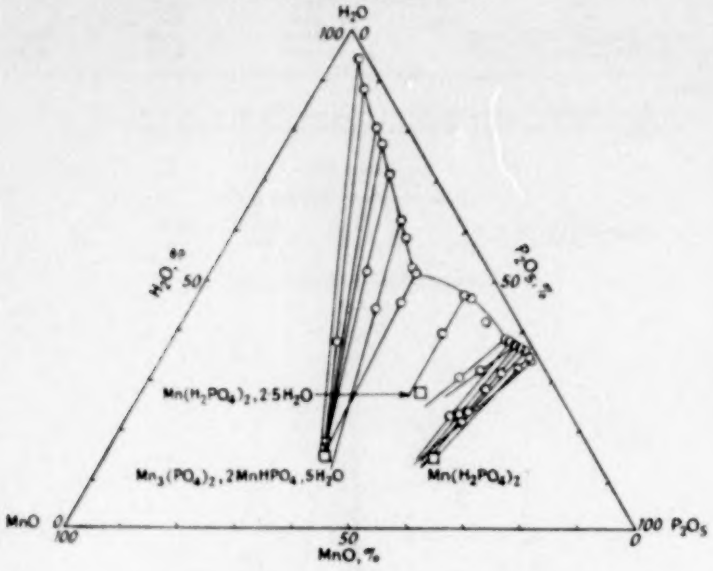
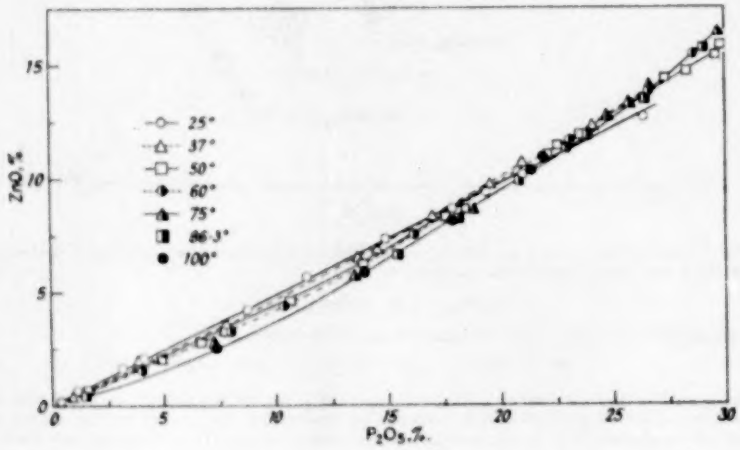


FIG. 5.

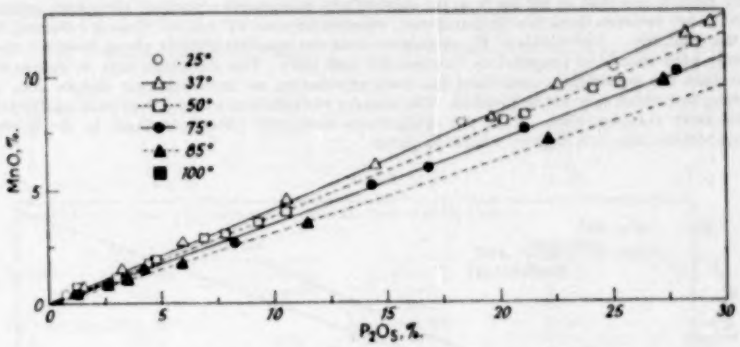


Evidence for a decrease in ionisation with rise of temperature comes from several sources. Noyes and Eastman (*Carnegie Inst. Publ.*, 1907, No. 63, 239—284) measured the conductivity of phosphoric acid solutions containing from 0·5 to 100 milliformula-weights/litre between 18° and 156°. They found that the value of $100\ \Lambda/\Lambda_0$ fell continuously with increasing temperature, and this may be taken to indicate a decrease in the degree of dissociation of the acid. Harned and Embree (*J. Amer. Chem. Soc.*, 1934, **56**, 1050) observed that the ionisation constants of weak acids pass through a maximum value with variation of temperature and conform to the equation

$$\log (K/K_{max.}) = -5{\cdot}0 \times 10^{-4}(t - \theta)^2$$

where t is the temperature (c.) and θ is the temperature corresponding to the value $K_{max.}$.

FIG. 6.



Nims (*ibid.*, p. 1110) determined the values of the first dissociation constant, K_1, of phosphoric acid between 0·3° and 50°. He obtained his results from e.m.f. measurements on cells without liquid junction, using the Debye–Hückel limiting equation to evaluate mean ionic activities. The variation of the first dissociation constant could, he found, be expressed by Harned and Embree's equation in the form

$$\log K_1 + 2{\cdot}0304 = -5 \times 10^{-4}(t + 18)^2$$

Thus the theoretical maximum value of K_1 would occur at $-18°$ and, above this, the ionisation would decrease with rise of temperature. Nims had earlier (*ibid.*, 1933, **55**, 1946) obtained values for the second dissociation constant between 20° and 50° and had discovered that this also passed through a maximum value—in this case at about 43°—so that above this temperature any effect related to the second stage of dissociation would in fact reinforce that due to the first stage.

If the decrease of solubility of the phosphates of zinc and manganese in dilute solutions is due to this decrease in the degree of ionisation of the acid, the same behaviour should be observed with the phosphates which separate from the more dilute solutions in the systems of other metals. The compositions of some saturated solutions in the ferrous phosphate system at 25° were determined, and in Fig. 7 there is a comparison with the data for the same system at 70° as given by Carter and Hartshorne (*J.*, 1926, 363). A decrease in solubility is again indicated. That the behaviour is not peculiar to the phosphates of bivalent metals is clear from the work of Carter and Hartshorne on the system ferric oxide–phosphoric oxide–water (*ibid.*, 1923, **123**, 2223). They found that the tertiary phosphate, $FePO_4.2\frac{1}{2}H_2O$, was much less soluble, and had a much greater range of stability, at 70° than at 25°.

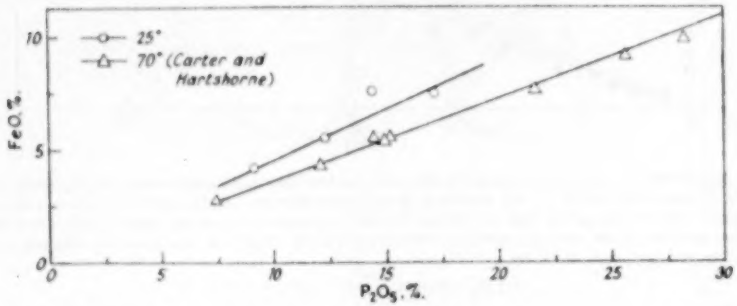
Additional evidence comes from the system calcium oxide–phosphoric oxide–water, investigated by Bassett (*Z. anorg. Chem.*, 1908, **59**, 1) and later by Elmore and Farr (*Ind. Eng. Chem.*, 1940, **32**, 580). They established that the secondary phosphate, $CaHPO_4$, which is the stable phase in contact with saturated solutions containing between 2% and about 20% of phosphoric oxide at 25°, shows a decrease in solubility as the temperature is increased to 100°. An increase in range of stability accompanies the solubility decrease.

Apparently few other systems have been fully examined, but the results quoted show that the effect has been observed with both bivalent and tervalent metals and also with secondary, secondary–tertiary, and tertiary phosphates. The only feature common to these phosphates is that they are the phases which separate from dilute solutions in their respective systems.

It is difficult to decide how far it is permissible to apply dissociation constants determined by the application of the Debye–Hückel limiting equation in explanation of effects observed in solutions of the concentration concerned in phase-diagram studies. The results of Noyes and Bray (*loc. cit.*) demonstrate that the decrease of ionisation with rise of temperature is still observable in M/10-phosphoric acid. It may occur in even more concentrated solutions although, if it does, the actual values of the dissociation constants will differ from those for dilute solutions.

Reference to Figs. 5 and 6 reveals that the solubilities in the zinc and the manganous systems do not fall proportionately to the rise of temperature. In each case, the solubility at 37° is only very slightly less than at 25° (in fact, the solubility of manganous secondary phosphate appears not to vary between these two temperatures), whereas between 37° and 50° there is a distinct fall in the solubility. The values of K_1, calculated from the equation already given, however, vary evenly with change of temperature between 25° and 100°. This difference may be due to the fact that the equilibrium concerned has been represented as involving only simple ions, an assumption which may not be justified. The primary phosphate in solution may be in equilibrium with more complex ions. With the manganous secondary phosphate there is the further complication that it is slightly soluble in water.

FIG. 7.



When discussing the results obtained by his method of "acidimetric precipitation," Rathje (*Ber.*, 1941, **74**, 342, 357, 546) attributed the separation of secondary phosphates from cold solutions and of tertiary phosphates from hot solutions, which his experiments indicated, to the slow rate of crystallisation of tertiary phosphates. He realised that bismuth tertiary phosphate must provide an exception, for it separates rapidly even from cold solutions, a fact utilised in the determination of phosphates. The chief weakness of his theory lies, however, in its inability to explain the decrease in solubility of such compounds as zinc tertiary phosphate, ferric tertiary phosphate, and calcium secondary phosphate which have been observed to separate from both hot and cold solutions. The present explanation seems to accord more closely with the known facts.

EXPERIMENTAL.

Preparation of Solutions for Phase-diagram Studies.—The various methods used were: (*a*) Dissolving the tertiary phosphate in the least possible quantity of phosphoric acid solution—at a temperature below the equilibrium temperature for the more dilute solutions or above it for the more concentrated solutions. (*b*) Dissolving the primary phosphate in water: in dilute solutions a clear metastable solution is first formed from which a more basic phosphate separates only on standing or on warming. (*c*) Dissolving zinc oxide in strong phosphoric acid (about 7M.) at temperatures between 50° and 100° to obtain a saturated solution and then diluting it: this method was not used with the manganous phosphates.

Although the solubility of manganous secondary phosphate varies only slightly with temperature, it is possible to use method (*a*) to prepare solutions in the region of the diagram where it forms the stable solid phase. The reason for this is that freshly diluted phosphoric acid will dissolve more manganous tertiary phosphate than it can retain in solution at room temperature or above.

None of these methods was suitable to obtain ferrous phosphate solutions. These were made from electrolytic iron (in slight excess) and phosphoric acid solution in an atmosphere of nitrogen.

Preparation of Tertiary Phosphates.—The tertiary phosphates were prepared from the metal sulphate according to the equation

$$3MSO_4,xH_2O + 2H_3PO_4 + 6NaOH = M_3(PO_4)_2,yH_2O + 3Na_2SO_4 + (6 + 3x - y)H_2O$$

About 100 g. of the sulphate, together with a slight excess of phosphoric acid, were dissolved in water and diluted to 600 ml. Vigorous stirring accompanied the dropwise addition of sodium hydroxide (1—2N.) until the solution was neutral to methyl-orange or only just faintly acid to litmus paper.

At room temperature this reaction gave either zinc tertiary phosphate tetrahydrate in the form of irregular prisms or a pinkish powder of hydrated manganous tertiary phosphate—the degree of hydration apparently depending on the concentration and on the temperature. At about 80°, the zinc tertiary phosphate appeared in the form of irregular plates, but, in the case of the manganous phosphate, the secondary–tertiary phosphate was precipitated instead of the tertiary compound.

Some typical analyses of zinc tertiary phosphate obtained by this method were :

	Temperature		Analysis.		
Sample.	of prepn.	of drying.	ZnO, %.	P_2O_5, %.	H_2O, %.
1	**room**	room	**53·4**	**30·8**	—
2	,,	40°	**53·2**	**30·9**	—
3	,,	40—45	**53·1**	**30·4**	**15·91**
4	,,	45—50	**52·8**	**30·6**	—
5	,,	50—55	**52·9**	**30·4**	
6	70—90°	**room**	**53·1**	**30·5**	—
Calc. for $Zn_3(PO_4)_2,4H_2O$			**53·28**	**30·99**	**15·74**

The following results were obtained for the manganous phosphates :

	Temperature		Analysis.		
Sample.	of prepn.	of drying.	MnO, %.	P_2O_5, %.	H_2O, %.
1	room	about 100°	**51·0**	**33·8**	—
2	,,	,,	**50·3**	**34·7**	—
Calc. for $Mn_3(PO_4)_2,3\frac{1}{2}H_2O$			**50·91**	**33·99**	**15·09**
3	room	room	**45·0**	**29·2**	**26·28**
4	,,	,,	**44·5**	**29·0**	—
5	,,	,,	**44·2**	**29·0**	—
Calc. for $Mn_3(PO_4)_2,7H_2O$			**44·24**	**29·53**	**26·23**
6	room	room	**24·4**	**16·0**	**59·1**
Calc. for $Mn_3(PO_4)_2,28H_2O$			**24·76**	**16·53**	**58·71**
7	70—80°	room	**46·9**	**37·5**	**14·46**
Calc. for $Mn_3(PO_4)_2,2MnHPO_4,5H_2O$			**47·49**	**38·04**	**14·47**

Sample (6) was prepared by the same method as the other samples but from solutions which were slightly more dilute.

Preparation of the Primary Phosphates.—A solution obtained by diluting 80 ml. of concentrated phosphoric acid with 20 ml. of water was saturated at room temperature with either zinc oxide or manganous tertiary phosphate. A slight excess of the oxide or phosphate was then added and dissolved by warming. On standing, crystals of the primary phosphate separated. They were carefully drained and were dried by pressing between filter paper.

Analysis of samples of zinc primary phosphate.

	ZnO, %.	P_2O_5, %.		ZnO, %.	P_2O_5, %.
Sample 1	**26·9**	**47·1**	Sample 2	**26·5**	**47·3**
Calc. for $Zn(H_2PO_4)_2,2H_2O$	27·5	48·1			

Analysis of samples of manganous primary phosphate.

	MnO, %.	P_2O_5, %.		MnO, %.	P_2O_5, %.
Sample 1	**23·9**	**48·6**	Sample 2	**24·1**	**48·3**
Calc. for $Mn(H_2PO_4)_2,2\frac{1}{2}H_2O$	24·12	48·31			

Materials.—All compounds and solutions were prepared from analytical grade materials. The tertiary phosphates obtained in the manner described were free from sodium.

Apparatus and Procedure.—The containers used were Monax boiling-tubes or flasks closed with rubber bungs. They were placed in a thermostat which was kept to within 0·1° of the chosen temperature. Normally they were shaken once a day. The most satisfactory method of detecting the attainment of equilibrium in the solutions proved to be repeated analysis. Changes in the conductivities and pH values of the solutions were observed to accompany crystallisation, but these did not provide a reliable enough indication. In practice it was necessary to make only one determination of the time required to reach equilibrium in a given range of concentration at a given temperature. It could be

applied to other solutions of the same order of concentration. If the analysis was not constant after 60 days, the experiment was abandoned.

The method of removal of successive samples was impracticable with ferrous phosphate solutions because they oxidise so rapidly in air. The solutions were given much longer to reach equilibrium than was known to be taken by the corresponding zinc and manganous phosphates and one analysis only was made—at the end of the period.

Solutions were left undisturbed for one or two days before removal of a sample. The solid phase had by then had time to sink to the bottom and to leave a completely clear supernatant liquor. Samples were taken by pipette (which gave an approximate value for the density) and were transferred to weighing bottles which were immediately stoppered. When it was certain that equilibrium had been reached, a sample of the moist solid phase was also analysed, if enough had crystallised out.

Analytical Methods.—Zinc was determined by titration with potassium ferrocyanide solution (approximately N/20)—the method used by Eberly, Gross, and Crowell. Neither the presence of phosphate nor that of perchloric acid (used in the phosphate determination) interfered with the procedure. It was found that, as recommended by Frost (*Analyst*, 1943, **68**, 51), *o*-dianisidine was a better indicator than diphenylamine for this titration.

Manganese was determined by potentiometric titration according to the method of Lingane and Karplus (*Ind. Eng. Chem. Anal.*, 1946, **18**, 191). It was found that the presence of orthophosphate did not interfere, neither did that, in small amounts, of perchloric acid.

Iron was determined by titration with standard potassium dichromate solution (approximately N/20). Since, after a short exposure to the air, the samples were partly oxidised, they were first reduced with stannous chloride in the usual manner.

Phosphate was determined by titration with standard bismuth oxyperchlorate solution (approximtely N/20). The method, which was developed by M. Hyams (unpublished work), depends on the precipitation of the phosphoric acid as bismuth phosphate. Bismuth oxyperchlorate solution is added to the phosphate solution, and the first excess of bismuth solution above that required to precipitate all the phosphoric acid is detected by means of thiourea (a yellow colour is produced). This procedure is similar to that described by Rathje (*Angew. Chem.*, 1938, **51**, 256) in which potassium iodide was employed as the indicator, but has the advantage that the titration may be carried out at slightly above room temperature instead of at the boiling temperature as with potassium iodide. Acids other than perchloric acid interfere with the titration, so that solid samples are first dissolved in that acid. The acid concentration is kept as low as possible. It was found that the presence of zinc and manganese in the amounts contained by the samples did not interfere. The titration could not, however, be carried out in the presence of iron and this had first to be removed by percolating the solution through a column of Permutit Zeo-Karb 215 ion exchange material.

The water present in the tertiary phosphates and in the manganous secondary–tertiary phosphate was determined by the loss on heating to constant weight, at dull red heat.

One of the authors (J. S.) thanks the Pyrene Company for a grant.

WILLIAM RAMSAY LABORATORY OF INORGANIC AND PHYSICAL CHEMISTRY, UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, May 20th*, 1950.]

---

547. *The Synthesis of Thyroxine and Related Substances. Part VII. The Preparation of Diphenyl Ethers from 2 : 6-Di-iodophenols.*

By J. H. BARNES, E. T. BORROWS, J. ELKS, B. A. HEMS, and A. G. LONG.

p-Halogenonitrobenzenes and *p*-nitrophenylpyridinium salts do not react with 2 : 6-di-iodophenols but the corresponding 2 : 4-dinitro-compounds give 2 : 6-di-iodo-2 : 4 -dinitrodiphenyl ethers. Attempts to reduce one or both of the nitro-groups of 3 : 5-di-iodo-4-(2 : 4-dinitrophenoxy)-*N*-acetyl-L-phenylalanine ethyl ester failed to yield a pure product. When 2 : 6-dinitrophenylpyridinium salts were treated with 2 : 6-di-iodophenols in hot pyridine, one iodine atom was lost and 2-iodo-2′ : 6′-dinitrodiphenyl ethers were produced. A 2 : 6-di-iodo-2′ : 6′-dinitrodiphenyl ether resulted from the reaction of methyl 4-chloro-3 : 5-di-nitrobenzoate and 3 : 5-di-iodo-*p*-cresol under mild conditions, but this method could not be applied to less highly activated halogeno-compounds.

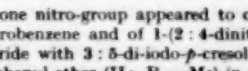
Attempts to prepare 2 : 6-di-iodophenyl ethers via di-iodoso- or di-iodoxy-phenols were unsuccessful. 4-Acetoxycyclohex-2-enyl ethers of 2 : 6-di-iodophenols were prepared but could not be dehydrogenated to 2 : 6-di-iodo-diphenyl ethers. 3 : 5-Di-iodo-4-(3-ketocyclohex-1-enyloxy)toluene was readily converted into 2 : 6-di-iodo-3′-hydroxy-4-methyldiphenyl ether by successive bromination, dehydrobromination, and rearrangement, but attempts to prepare the 4′-hydroxy-compound by similar means were unsuccessful.

THE difficulties associated with the synthesis of thyroxine have been largely caused by the lack of convenient methods for the preparation of 2 : 6-di-iododiphenyl ethers. Harington and Barger (*Biochem. J.*, 1927, **21**, 169) in their original synthesis of the hormone built up this system by reaction of 3 : 4 : 5-tri-iodonitrobenzene with *p*-methoxyphenol, but were then faced

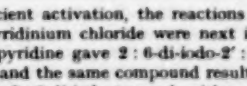
with the elaboration of an α-alanine side-chain from an aromatic nitro-group. An attempt to simplify this process (Part I of this series; Borrows, Clayton, and Hems, *J.*, 1949, S 185) failed because neither 4-chloro-3 : 5-di-iodobenzoic acid nor its methyl ester could be made to react with quinol or its monomethyl ether. The syntheses of DL- and L-thyroxine reported in previous papers of this series (*J.*, 1949, 3424, S 185, S 190, S 199) have depended on the preparation of 2 : 6-dinitrodiphenyl ethers from halogeno-2 : 6-dinitrobenzenes or 2 : 6-dinitrophenols and the replacement of the nitro-groups by iodine atoms *via* the diamines. These methods have allowed the use as starting materials of tyrosine or its derivatives in which the required side chain is already present and convenient syntheses of thyroxine have been devised, but one of our aims throughout this work has been to find a more direct method, proceeding *via* 3 : 5-di-iodotyrosine which is very readily available.

The only method so far described for the preparation of diphenyl ethers from 2 : 6-di-iodophenols is the oxidation, under mild conditions, of 3 : 5-di-iodotyrosine or its derivatives to the corresponding derivative of thyroxine (see Harington, *J.*, 1944, 193, for earlier references; Harington and Pitt Rivers, *Biochem. J.*, 1945, **39**, 157; Pitt Rivers, *ibid.*, 1948, **43**, 223; Turner and Reineke, U.S.P. 2,435,947; Every, B.P. 598,691). By selection of a suitable derivative of 3 : 5-di-iodotyrosine this method can be made to give thyroxine in fair yield (Pitt Rivers, *loc. cit.*), but it is very inflexible; apart from simple derivatives of 3 : 5-di-iodotyrosine, the only compound that has been used successfully is the related β-(3 : 5-di-iodo-4-hydroxyphenyl)lactic acid (Saul and Trikojus, *Biochem. J.*, 1948, **42**, 80).

Attempts to prepare ethers by treatment of 2 : 6-di-iodophenols with aryl halides have been described by Harington and Barger (*loc. cit.*), by Canzanelli, Harington, and Randall (*ibid.*, 1934, **28**, 68), and by Borrows, Clayton, and Hems (*J.*, 1949, S 185), but even as reactive a halide as *p*-iodonitrobenzene failed to react. *p*-Fluoronitrobenzene was shown by Rarick, Brewster, and Dains (*J. Amer. Chem. Soc.*, 1933, **55**, 1289) to be particularly reactive towards rather inert phenols but we have been unable to prepare 2 : 6-di-iodo-4′-nitro-4-methyldiphenyl ether (I; R = NO_2) from this fluoro-compound and 3 : 5-di-iodo-*p*-cresol.



(I.)



(II.)

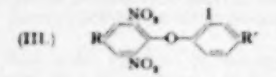
Since one nitro-group appeared to cause insufficient activation, the reactions of 1-chloro-2 : 4-dinitrobenzene and of 1-(2 : 4-dinitrophenyl)pyridinium chloride were next investigated. This chloride with 3 : 5-di-iodo-*p*-cresol in boiling pyridine gave 2 : 6-di-iodo-2′ : 4′-dinitro-4-methyldiphenyl ether (II; R = Me) in 62% yield, and the same compound resulted from the reaction between 1-chloro-2 : 4-dinitrobenzene and 3 : 5-di-iodo-*p*-cresol, either in alcoholic sodium ethoxide or in methyl ethyl ketone in the presence of potassium carbonate. By one or other of these methods the diphenyl ethers, (II; R = CHO, CO_2Me, and $CH_2{\cdot}CH_2{\cdot}CO_2Et$), were also prepared.

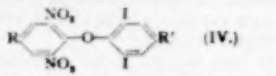
Attention was next turned to the preparation of diphenyl ethers from 3 : 5-di-iodotyrosine. Previous experience suggested that both the amino- and the carboxy-group should be protected and the derivative chosen was 3 : 5-di-iodo-*N*-acetyltyrosine ethyl ester, the preparation of which from 3 : 5-di-iodo-L-tyrosine has been improved (see Experimental section). Both the L- and the DL-ester lost iodine on crystallisation, but this could be prevented by the presence of a little mineral acid. An attempt to prepare the L-acetamido-ester directly from 3 : 5-di-iodo-*ON*-diacetyl-L-tyrosine was unsuccessful; esterification of this compound in chloroform solution left the acetoxy-group intact and the resulting 3 : 5-di-iodo-*ON*-diacetyl-L-tyrosine ethyl ester was stable to boiling alcoholic hydrogen chloride.

The acetamido-esters were converted into the corresponding 3 : 5-di-iodo-4-(2′ : 4′-dinitrophenoxy)-*N*-acetylphenylalanine ethyl esters [II; R = $CH_2{\cdot}CH(NHAc){\cdot}CO_2Et$] by the usual method. A number of attempts were made to reduce, selectively, the 2-nitro-group of [II; R = L-$CH_2{\cdot}CH(NHAc){\cdot}CO_2Et$] both with stannous chloride and with alkali sulphides under various conditions, but no crystalline product could be isolated. Attempts to reduce the dinitro-compound to the diamine with stannous chloride or titanous chloride also gave impure material.

It seemed probable that halogeno-2 : 6-dinitrobenzenes and 1-(2 : 6-dinitrophenyl)pyridinium salts would behave in much the same way as their 2 : 4-dinitro-analogues and some model experiments were carried out. When 1-(2 : 6-dinitro-4-methylphenyl)pyridinium toluene-*p*-sulphonate was treated with 3 : 5-di-iodo-4-hydroxybenzaldehyde in boiling pyridine, the only

solid product, which was isolated in small yield, was 3-iodo-4-(2 : 6-dinitro-4-methylphenoxy)-benzaldehyde (III; R = Me, R′ = CHO). Treatment of the material with morpholine at 100° gave 3-iodo-4-hydroxybenzaldehyde and 3 : 5-dinitro-4-morpholinotoluene, the latter being also prepared from morpholine and 4-chloro-3 : 5-dinitrotoluene. For comparison the 3-iodo-4-hydroxybenzaldehyde was prepared very conveniently by addition of iodine to *p*-hydroxybenzaldehyde in dimethylamine solution. Treatment of the monoiodo-aldehyde in pyridine solution with 1-(2 : 6-dinitro-4-methylphenyl)pyridinium toluene-*p*-sulphonate gave (III; R = Me, R′ = CHO) identical with the material obtained as described above.


(III.)

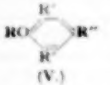

(IV.)

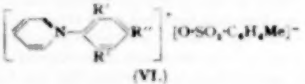
This rather remarkable loss of an iodine atom has been observed in reactions between 1-(2 : 6-dinitro-4-methylphenyl)pyridinium toluene-*p*-sulphonate and 3 : 5-di-iodo-*p*-cresol, between 1-(2 : 6-dinitro-4-carbomethoxyphenyl)pyridinium chloride and methyl 3 : 5-di-iodo-4-hydroxybenzoate, and between 1-(2 : 6-dinitro-4-methoxyphenyl)pyridinium toluene-*p*-sulphonate and 3 : 5-di-iodo-*p*-cresol, pyridine at 100° being used as solvent. From each only one compound could be obtained pure and this in very poor yield. Analysis indicated an iodine : nitrogen ratio of 1 : 2 and, by analogy, the products of these three reactions are regarded as having the structures (III; R = R′ = Me), (III; R = R′ = CO_2Me), and (III; R = OMe, R′ = Me), respectively.

Although this loss of iodine might appear to be related to the difficulty in accommodating four bulky groups in the positions *ortho* to the oxygen atom, it has nevertheless been possible to prepare a 2 : 6-di-iodo-2′ : 6′-dinitrodiphenyl ether by employing less vigorous conditions; thus, methyl 4-chloro-3 : 5-dinitrobenzoate with 3 : 5-di-iodo-*p*-cresol in the presence of potassium carbonate in methyl ethyl ketone gave a fair yield of a compound giving the correct analysis for methyl 3 : 5-dinitro-4-(2 : 6-di-iodo-4-methylphenoxy)benzoate (IV; R = CO_2Me, R′ = Me). On prolonged heating with morpholine this gave 3 : 5-di-iodo-*p*-cresol, showing that there had been no migration of the iodine atoms.

Attempts to prepare (IV; R = R′ = Me) by reaction of 4-chloro-3 : 5-dinitrotoluene with 3 : 5-di-iodo-*p*-cresol under similar conditions were unsuccessful, and it seems probable that the ability of methyl 4-chloro-3 : 5-dinitrobenzoate to undergo the reaction depends on the extra activation of the chlorine atom by the *p*-carbomethoxy-group.

There are some indications in the literature (Vorländer, *Ber.*, 1925, **58**, 1893; Masson, Race and Pounder, *J.*, 1935, 1669) that iodoxy-groups, like nitro-groups, are electrophilic, and the possibility arose of obtaining diphenyl ethers from 2 : 6-di-iodoso- (V; R = H, R′ = IO) or 2 : 6-di-iodoxyphenols (V; R = H, R′ = IO_2) *via* their toluene-*p*-sulphonic esters and the quaternary salts (VI; R′ = IO or IO_2). Reduction of the product would then give a 2 : 6-di-iododiphenyl ether.


(V.)

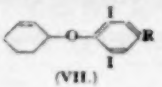

(VI.)

Attempts to prepare di-iodoxy-compounds by direct oxidation of either 3 : 5-di-iodo-*p*-cresol or 3 : 5-di-iodo-*p*-cresyl toluene-*p*-sulphonate with Caro's acid (Bamberger and Hill, *Ber.*, 1900, **33**, 533) were unsuccessful, the iodo-compounds being recovered unchanged.

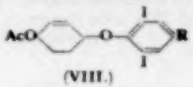
Treatment of the esters (V; R = *p*-C_6H_4Me·SO_2, R′ = I, R″ = Me or CO_2Me) with chlorine in aqueous pyridine (Ortoleva, *Gazzetta*, 1900, **30**, (ii), 1) or in chloroform (King and McCombie, *J.*, 1913, **220**) led to chlorinated products, from which no pure compounds could be obtained; the products reverted to the parent di-iodo-compounds on treatment with sodium hypochlorite or with alkali.

Another approach arose from the knowledge that 2 : 6-di-iodophenols, although they do not form ethers with simple aromatic halides, form aliphatic ethers readily. An appropriately substituted *cyclo*hexenyl ether (*e.g.*, VIII) could subsequently be converted into a diaryl ether (IX) by dehydrogenation. Consequently, the preparation of unsaturated ethers of 3 : 5-di-iodophenols was studied with allyl bromide and 3-bromo*cyclo*hexene. Neither of these compounds yielded ethers (*e.g.*, VII) on treatment with 3 : 5-di-iodo-*N*-acetyl-DL-tyrosine in

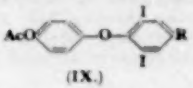
aqueous alkaline solution, but they did so in alcoholic sodium ethoxide or in methyl ethyl ketone containing potassium carbonate. Similarly were prepared the ethers (VII; R = CO_2Me, Me, and CHO), which were required for the study of methods of dehydrogenation.



(VII.)



(VIII.)



(IX.)

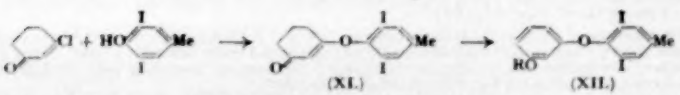
The action of selenium dioxide on some of the above-mentioned ethers was investigated with the object of introducing a hydroxyl or ketonic group at the 4'-position. Treatment of (VII; R = CO_2Me) with selenium dioxide in **95%** acetic acid, aqueous alcohol, or aqueous dioxan caused loss of iodine and gave an unidentified selenium-containing compound that could not readily be purified. Guillemonat (*Ann. Chim.*, **1939**, **11**, 143; *Compt. rend.*, **1937**, **205**, 67) converted *cyclo*hexene into 3-acetoxy*cyclo*hexene by treatment with selenium dioxide in a mixture of acetic acid and acetic anhydride; however, (VII; R = Me or CO_2Me) with acetic anhydride, with or without selenium dioxide, gave only the acetate of the parent di-iodo-phenol. This interesting reaction appears to be related to the presence of the iodine atoms, since 3-phenoxy*cyclo*hexene is unaffected by acetic anhydride. The reaction apparently does not proceed through the di-iodophenols, as these compounds are not acetylated under the conditions of the reaction.

Since the *cyclo*hex-2-enyl ethers were such unpromising intermediates, attention was turned to the 4'-acetoxy-compounds (VIII); these were prepared from 3-bromo-6-acetoxy*cyclo*hexene, which with methyl 3 : 5-di-iodo-4-hydroxybenzoate or 3 : 5-di-iodo-*p*-cresol in methyl ethyl ketone in the presence of potassium carbonate gave the ethers (VIII; R = CO_2Me or Me), respectively.

The 4'-acetoxy*cyclo*hex-2'-enyl ethers (VIII; R = CO_2Me or Me) are fairly stable to heat, being recovered almost quantitatively after several hours' heating in boiling xylene, although the *cyclo*hex-2-enyl ethers were rather rapidly decomposed by this treatment. An attempt to dehydrogenate (VIII; R = Me) by chloranil in boiling xylene was unsuccessful, only traces of phenolic material being produced after hydrolysis of the crude product. This failure was not merely due to the presence of iodine in the molecule, for even the simple analogue, 3-phenoxy-*cyclo*hexene, gave no appreciable quantity of diphenyl ether on such treatment. An attempt to convert (VIII; R = Me) into the diphenyl ether (IX; R = Me) by bromination-dehydrobromination was equally unsuccessful; treatment with two equivalents of *N*-bromosuccinimide in the presence of potassium acetate (cf. Barnes, *J. Amer. Chem. Soc.*, **1948**, **70**, 145) gave a small quantity of halogen-free material as the only pure product.

We next turned our attention to the 4-keto*cyclo*hex-2-enyl ethers (X) of di-iodophenols, which require the removal of only two hydrogen atoms to give 2 : 6-di-iodo-4'-hydroxydiphenyl ethers. The preparation of compounds of type (X) promised to be difficult, and preliminary experiments were therefore carried out with the more readily accessible 3-keto*cyclo*hex-1-enyl ethers.

(X.)

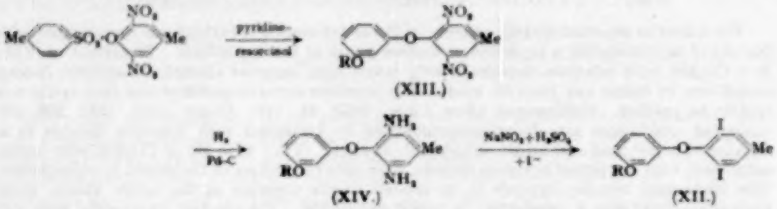


(XI.) (XII.)

3-Chloro*cyclo*hex-2-enone (Crossley and Haas, *J.*, **1903**, **494**) was treated with 3 : 5-di-iodo-*p*-cresol in methyl ethyl ketone in the presence of potassium carbonate, yielding 3 : 5-di-iodo-4-(3-keto*cyclo*hex-1-enyloxy)toluene (XI); this was fairly stable, being recovered in good yield after 2 hours in boiling xylene or after 24 hours in acetic anhydride at 100°. It was unaffected by palladised charcoal in boiling xylene or by selenium dioxide in boiling alcohol or aqueous alcohol. However, it reacted with selenium dioxide in acetic acid, either pure or aqueous, as shown by the quantitative liberation of selenium. Because the required phenol (XII; R = H), which had been prepared by a different route (see below), was known to be unstable to selenium dioxide, the oxidation of (XI) was then attempted with selenium dioxide in a mixture of acetic acid and acetic anhydride in order that any phenolic material formed

should be protected from further oxidation by acetylation. However, although selenium was formed there was no evidence of the presence among the reaction products of the expected diphenyl ether (XII; R = Ac). Dehydrogenation of (XI) was finally achieved by successive bromination and dehydrobromination (*N*-bromosuccinimide, then 2 : 4 : 6-collidine), subsequent acetylation affording (XII; R = Ac) in 77% yield [based on (XI)].

In an alternative synthesis of (XII; R = Ac) the methods used were similar to those described in earlier papers in this series:



Treatment of 3 : 5-dinitro-*p*-tolyl toluene-*p*-sulphonate with resorcinol in pyridine gave some *m*-di-(2′ : 6′-dinitro-4′-methylphenoxy)benzene as an alkali-insoluble fraction and, as the main product, 2 : 6-dinitro-3′-hydroxy-4-methyldiphenyl ether (XIII; R = H) as an oil, best purified by way of its solid acetate. Hydrogenation of the acetate (XIII; R = Ac) in the presence of palladised charcoal gave the diamine (XIV; R = Ac), which (crude) was tetrazotised, etc., yielding the di-iodo-compound (XII; R = Ac) in rather poor yield.

Attempts to apply this method to the preparation of 2 : 6-di-iodo-4′-hydroxydiphenyl ethers failed. Treatment of *cyclo*hex-2-enone with *N*-bromosuccinimide gave an extremely unstable product which with 3 : 5-di-iodo-*p*-cresol afforded a small quantity of an oily ketone. This appeared, from the composition of the 2 : 4-dinitrophenylhydrazone, to be (X) or an isomer but could not be dehydrogenated to the corresponding diphenyl ether by any of the usual methods.

The failure of so many attempts to prepare thyroxine from di-iodophenols, together with the development of the rather convenient preparation of L-thyroxine described in Part V (*J.*, 1949, 3424), has now led us to abandon this line of research.

Experimental.

2 : 6-Di-iodo-2′ : 4′-dinitro-4-methyldiphenyl Ether.—(*a*) 1-Chloro-2 : 4-dinitrobenzene (2·02 g.) and pyridine (20 ml.) were heated together on the water-bath till separation of solid was complete. 3 : 5-Di-iodo-*p*-cresol (10 g.) was added and the mixture boiled under reflux for 90 minutes. The solution was poured into an excess of dilute hydrochloric acid, and the aqueous layer decanted from the lower oily layer. The oil solidified on treatment with 2*N*-sodium hydroxide and was filtered off, washed with water, and crystallised from aqueous acetic acid. In order to remove dark impurities a solution of the material in acetone was passed through a short column of alumina, acetone being used for elution. After removal of the solvent the *diphenyl ether* (3·3 g., 62%) crystallised from glacial acetic acid in pale yellow prisms, m. p. 200—202° (Found: N, 5·4; I, 48·5. $C_{19}H_8O_5N_2I_2$ requires N, 5·3; I, 48·25%).

(*b*) Sodium (0·23 g.) was dissolved in absolute ethanol (15 ml.), 1-chloro-2 : 4-dinitrobenzene (2·03 g.) and 3 : 5-di-iodo-*p*-cresol (3·6 g.) were added, and the solution was boiled under reflux for 90 minutes. The solution was poured into water, and the solid was filtered off and purified as above, to give 2·5 g. (47%) of the diphenyl ether, m. p. 200°.

(*c*) A mixture of 1-chloro-2 : 4-dinitrobenzene (1·0 g.), 3 : 5-di-iodo-*p*-cresol (1·8 g.), potassium carbonate (1·38 g.), and methyl ethyl ketone (20 ml.) was boiled under reflux for 1 hour. After cooling, the mixture was filtered and the filtrate evaporated. The residual crystalline solid crystallised from glacial acetic acid as prisms (1·3 g., 50%) melting at 200—202°.

3 : 5-Di-iodo-4-(2′ : 4′-dinitrophenoxy)benzaldehyde.—This compound was prepared from 1-chloro-2 : 4-dinitrobenzene (1·10 g.), 3 : 5-di-iodo-4-hydroxybenzaldehyde (2·8 g.), and pyridine (10 ml.) as in method (*a*) above. The *aldehyde* separated from glacial acetic acid as almost colourless prisms (1·3 g., 48%), m. p. 258—259° (decomp.) (Found: N, 3·0. $C_{13}H_6O_6N_2I_2$ requires N, 3·2%).

Methyl 3 : 5-Di-iodo-4-(2′ : 4′-dinitrophenoxy)benzoate.—A mixture of 1-fluoro-2 : 4-dinitrobenzene (1·86 g.), methyl 3 : 5-di-iodo-4-hydroxybenzoate (4·04 g.), potassium carbonate (2·76 g.), and methyl ethyl ketone (25 ml.) was boiled under reflux for 1 hour. After cooling, the mixture was filtered and the filtrate was evaporated to dryness. The residual solid was washed with 2*N*-sodium hydroxide and was then crystallised from aqueous ethanol. The *diphenyl ether* separated as yellow prisms (3·2 g., 56%) melting at 181—182° (Found: N, 3·1; I, 44·5. $C_{14}H_8O_7N_2I_2$ requires N, 4·9; I, 44·5%).

β-(3 : 5-Di-iodo-4-hydroxyphenyl)propionic Acid.—A solution of iodine (50 g.) and potassium iodide (48 g.) in water (150 ml.) was added gradually to a stirred solution of *β-p*-hydroxyphenylpropionic acid

(16·2 g.) in aqueous methylamine (20%; 200 ml.). When the addition was complete the mixture was stirred for a further 10 minutes and was then acidified to Congo-red by the gradual addition of 2N-hydrochloric acid. The white solid was filtered off, washed with water, and dried. Recrystallisation from ethanol yielded the di-iodo-compound as colourless needles (38 g., 90%), m. p. 166—168° (decomp.) (Found: C, 26·2; H, 2·2; I, 60·9. Calc. for $C_9H_9O_3I_2$: C, 25·9; H, 1·9; I, 60·7%). Bougault (*Compt. rend.*, 1900, **131**, 43) gives m. p. 162°.

The *ethyl* ester was prepared in 84% yield by esterification of the acid in chloroform solution with toluene-*p*-sulphonic acid as catalyst, water being removed azeotropically. It crystallised from ethanol as white prisms, m. p. 86—88° (Found: C, 29·8; H, 2·9; I, 57·0. $C_{11}H_{13}O_3I_2$ requires C, 29·6; H, 2·7; I, 56·9%).

Ethyl β-[3 : 5-*Di-iodo*-4-(2′ : 4′-*dinitrophenoxy*)*phenyl*]*propionate*.—Ethyl β-(3 : 5-di-iodo-4-hydroxyphenyl)propionate (4·46 g.) was added to 1-(2 : 4-dinitrophenyl)pyridinium bromide, prepared by heating 1-bromo-2 : 4-dinitrobenzene (1·24 g.) with pyridine (20 ml.) at 100° for 30 minutes. The mixture was heated on the water-bath for 2 hours and the product isolated in the usual way. The *diphenyl ether* crystallised from acetic acid as yellowish prisms (1·2 g., 39%), m. p. 128—130° (Found: N, 4·5; I, 40·9. $C_{17}H_{14}O_7N_2I_2$ requires N, 4·6; I, 41·5%).

3 : 5-*Di-iodo*-L-*tyrosine*.—A solution of iodine (320 g.) and sodium iodide (400 g.) in water (1·3 l.) was added dropwise to a stirred solution of L-tyrosine (100 g.) in 20% aqueous ethylamine (1 l.). When the addition was complete the mixture was stirred for a further 30 minutes. Excess of iodine was removed by treatment with sodium pyrosulphite, and the amino-acid was precipitated by adjustment of the pH to 5—6 with acetic acid. The solid was filtered off, washed with water, and purified by dissolution in N-hydrochloric acid and re-precipitation with ammonia. The yield was 200 g. (75%).

3 : 5-*Di-iodo*-N-*acetyl*-L-*tyrosine*.—A solution of **3** : 5-di-iodo-L-tyrosine (167 g.) in 2N-sodium hydroxide (1670 ml.) was kept between 5° and 10° and stirred while acetic anhydride (184 ml.) was added during 1 hour. After being kept overnight the solution was treated with sodium hydroxide (80 g.) in water (200 ml.) and left at room temperature for 3 hours. After addition of alcohol (1 l.) the solution was stirred and acidified to pH 2 by means of concentrated hydrochloric acid. The solid was filtered off and washed with water; a small second crop was obtained by dilution of the filtrate. The acetamido-acid (159 g., 87%) melted at 112—118°, and was used without further purification.

3 : 5-*Di-iodo*-N-*acetyl*-L-*tyrosine Ethyl Ester*.—**3** : 5-Di-iodo-*N*-acetyl-L-tyrosine (158 g.), toluene-*p*-sulphonic acid (10 g.), ethanol (100 ml.), and chloroform (1 l.) were boiled together under reflux for 8 hours, water being separated automatically from the azeotrope. After cooling, the solution was washed with sodium hydrogen carbonate solution, then with water, and was evaporated to dryness. The residual solid was crystallised from aqueous ethanol containing a few drops of hydrochloric acid. The *ethyl* ester was obtained as colourless needles (147·5 g., 88%), m. p. 154—155°, $[\alpha]_D^{20}$ +15·4° (*c*, 2·0 in ethanol) (Found: C, 31·3; H, 3·2; N, 2·5; I, 52·0. $C_{13}H_{15}O_4NI_2$ requires C, 31·0; H, 3·0; N, 2·8; I, 50·5%).

3 : 5-*Di-iodo*-N-*acetyl*-DL-*tyrosine Ethyl Ester*.—This compound was prepared from **3** : 5-di-iodo-*N*-acetyl-DL-tyrosine by the method described above for the L-compound. The *ester* was obtained as small white needles (89%), m. p. 145—146° (Found: N, 2·9; I, 50·9. $C_{13}H_{15}O_4NI_2$ requires N, 2·8; I, 50·5%).

3 : 5-*Di-iodo*-O*N*-*diacetyl*-L-*tyrosine Ethyl Ester*.—**3** : 5-Di-iodo-*ON*-diacetyl-L-tyrosine (Myers, *J. Amer. Chem. Soc.*, 1932, **54**, 3718) (5·2 g.) was esterified in the usual way by treatment with ethanol (3 ml.) in chloroform (120 ml.) with toluene-*p*-sulphonic acid (2 g.) as catalyst. The *ethyl* ester crystallised from benzene–light petroleum in colourless prisms, m. p. 109—112°, $[\alpha]_D^{20}$ +27° (*c*, 1·4 in ethanol) (Found: C, 32·8; H, 3·0. $C_{15}H_{17}O_5NI_2$ requires C, 33·0; H, 3·0%).

3 : 5-*Di-iodo*-4-(2′ : 4′-*dinitrophenoxy*)-N-*acetyl*-L-*phenylalanine Ethyl Ester*.—**3** : 5-Di-iodo-*N*-acetyl-L-tyrosine ethyl ester (50 g.), 1-chloro-2 : 4-dinitrobenzene (20 g.), potassium carbonate (28 g.), and methyl ethyl ketone (400 ml.) were boiled together under reflux for 1 hour. The mixture was filtered and the filtrate evaporated to dryness. The residue was dissolved in benzene and the solution was washed with sodium hydroxide solution and with water. The gum left on evaporation of the solvent was dissolved in a very little methanol and treated with warm ether. On cooling, the *diphenyl ether* (57 g., 82%) separated as a solvate, m. p. 102—104°. The material lost its solvent at 110°/10 mm. and then had the correct analysis (Found: C, 34·3; H, 2·7. $C_{18}H_{17}O_8N_3I_2$ requires C, 34·1; H, 2·5%). $[\alpha]_D^{20}$ was +5·9° (*c*, 2·0 in alcohol). The solvent-free material could not be recrystallised from any of the usual solvents.

3 : 5-*Di-iodo*-4-(2′ : 4′-*dinitrophenoxy*)-N-*acetyl*-L-*phenylalanine*.—A solution of the above ester (10 g.) in alcohol (50 ml.) was treated with a solution of potassium hydroxide (5·6 g.) in alcohol (50 ml.). After 10 minutes the solution was poured into water (500 ml.), and the solution was acidified with hydrochloric acid. Crystallisation of the solid from aqueous alcohol gave the *acetamido-acid* (8 g., 84%) melting at 210—212°, $[\alpha]_D^{20}$ +12° (*c*, 1·0 in 90% ethanol) (Found: C, 31·9; H, 2·2; N, 6·7. $C_{17}H_{13}O_8N_3I_2$ requires C, 31·8; H, 2·0; N, 6·55%).

3 : 5-*Di-iodo*-4-(2′ : 4′-*dinitrophenoxy*)-L-*phenylalanine Hydrochloride*.—A solution of the acetamido-ester (5 g.) in a mixture of glacial acetic acid (20 ml.) and concentrated hydrochloric acid (20 ml.) was refluxed for 6 hours. Yellow needles separated on cooling, which changed to a colourless powder when washed with water. This powder dissolved readily in hot acetic acid and the *amino-acid hydrochloride* separated rapidly as pale yellow needles, m. p. 212—216°, $[\alpha]_D^{20}$ +5·6° (*c*, 0·63 in ethanol) (Found: C, 28·2; H, 2·1. $C_{15}H_{11}O_7N_3ClI_2$ requires C, 28·2; H, 1·9%).

3 : 5-*Di-iodo*-4-(2′ : 4′-*dinitrophenoxy*)-N-*acetyl*-DL-*phenylalanine Ethyl Ester*.—(*a*) **3** : 5-Di-iodo-*N*-acetyl-DL-tyrosine ethyl ester (2·5 g.) and pyridine (5 ml.) were added to 1-(2 : 4-dinitrophenyl)pyridinium chloride prepared from 1-chloro-2 : 4-dinitrobenzene (0·5 g.) and pyridine (5 ml.); the mixture was heated on the steam-bath for 2 hours and the product isolated in the usual way. The *diphenyl ether*

crystallised from aqueous acetic acid as a white powder (1·0 g., 60%) melting at 204—206° (Found: C, 34·4; H, 2·6; N, 6·1; I, 38·7. $C_{16}H_{11}O_4N_3I_2$ requires C, 34·1; H, 2·5; N, 6·3; I, 38·0%).

(*b*) 1-Chloro-2 : 4-dinitrobenzene (2·03 g.), 3 : 5-di-iodo-*N*-acetyl-DL-tyrosine ethyl ester (5·03 g.), potassium carbonate (2·76 g.), and methyl ethyl ketone (40 ml.) were boiled together under reflux for 1 hour. The hot solution was filtered and the filtrate, on cooling, deposited a white powder melting at 202—204°. A further quantity was obtained by concentration of the mother-liquors. Crystallisation from aqueous acetic acid and finally from a mixture of acetone and light petroleum (b. p. 60—80°) gave material (5·5 g., 82%), m. p. 204—206°.

Reaction of 1-(2 : 6-*Dinitro*-4-*methylphenyl*)*pyridinium Toluene*-p-*sulphonate with* 3 : 5-*Di-iodo*-4-*hydroxybenzaldehyde*.—A solution of the quaternary salt (Borrows, Clayton, Hems, and Long, *J.*, 1949, S 190) (8·6 g.) and 3 : 5-di-iodo-4-hydroxybenzaldehyde (15 g.) in pyridine (50 ml.) was boiled under reflux for 1 hour and the solution was then cooled and poured on a mixture of 2*N*-hydrochloric acid and ice. The deposited oil was taken up in chloroform, and the solution was washed successively with 2*N*-hydrochloric acid, 2*N*-sodium hydroxide, and water, and was then evaporated to small bulk. The chloroform solution was poured on an alumina column which was washed with more chloroform. On evaporation of the eluate a brown syrup was obtained which crystallised on storage and, on recrystallisation from aqueous acetic acid, gave 3-*iodo*-4-(2′ : 6′-*dinitro*-4′-*methylphenoxy*)*benzaldehyde* as greenish prisms (3·1 g., 36%), m. p. 159—160° (Found: N, 6·4; I, 29·5. $C_{14}H_8O_6N_2I$ requires N, 6·5; I, 29·7%).

The compound (2·5 g.) was heated with morpholine (10 ml.) on the water-bath for 2 hours and the solution was poured on excess of 2*N*-hydrochloric acid and ice. The deposited oil was taken up in chloroform and the chloroform solution was extracted repeatedly with sodium hydrogen carbonate solution. The carbonate extract, on acidification, gave 3-iodo-4-hydroxybenzaldehyde, m. p. 113—115°, undepressed on admixture with an authentic specimen. Evaporation of the chloroform solution gave an oil which crystallised from ethanol as orange needles, m. p. 127—129°, undepressed on admixture with a specimen of 3 : 5-dinitro-4-morpholinotoluene prepared as described below.

3 : 5-*Dinitro*-4-*morpholinotoluene*.—A mixture of 4-chloro-3 : 5-dinitrotoluene (0·19 g.) and morpholine (1 ml.) was heated on the steam-bath for 90 minutes, cooled, and poured into excess of 2*N*-hydrochloric acid and ice. The precipitate crystallised from ethanol as long orange needles (0·21 g., 90%), m. p. 127—129° (Found: C, 49·4; H, 5·0; N, 15·4. $C_{11}H_{13}O_5N_3$ requires C, 49·4; H, 4·9; N, 15·7%).

3-*Iodo*-4-*hydroxybenzaldehyde*.—A solution of iodine (25·4 g.) and potassium iodide (22 g.) in water (300 ml.) was added to *p*-hydroxybenzaldehyde (12·2 g.) in aqueous dimethylamine (100 ml., 30%), with stirring, during 90 minutes. The dark precipitate was filtered off and the filtrate acidified by the addition of 2*N*-hydrochloric acid. Crystallisation of the precipitated solid from hot water gave colourless leaflets, m. p. 113—115° (Found: C, 34·1; H, 2·1; I, 51·5. Calc. for $C_7H_5O_2I$: C, 33·9; H, 2·0; I, 51·2%). Paal (*Ber.*, 1895, **28**, 2407) gives m. p. 108°.

The 2 : 4-*dinitrophenylhydrazone* crystallised from aqueous acetic acid as an orange-red powder, m. p. 269—271° (decomp.) (Found: N, 12·8; I, 30·65. $C_{13}H_9O_5N_4I$ requires N, 13·1; I, 29·6%).

Unambiguous Synthesis of 3-*Iodo*-4-(2′ : 6′-*dinitro*-4′-*methylphenoxy*)*benzaldehyde*.—A solution of 1-(2 : 6-dinitro-4-methylphenyl)pyridinium toluene-*p*-sulphonate (2·15 g.) and 3-iodo-4-hydroxybenzaldehyde (1·24 g.) in pyridine (20 ml.) was boiled under reflux for 1 hour. After cooling, the mixture was poured into 2*N*-hydrochloric acid containing ice, and the deposited syrup was taken up in chloroform and washed successively with 2*N*-hydrochloric acid, 2*N*-sodium hydroxide, and water. The chloroform solution was evaporated to small bulk and poured on an alumina column. The material was eluted with chloroform and, after removal of the solvent, was crystallised from aqueous acetic acid. The compound (0·65 g., 30%) melted at 159—160° and did not depress the m. p. of the material prepared from 3 : 5-di-iodo-4-hydroxybenzaldehyde.

2′-*Iodo*-2 : 6-*dinitro*-4 : 4′-*dimethyldiphenyl Ether*.—This was prepared from 1-(2 : 6-dinitro-4-methylphenyl)pyridinium toluene-*p*-sulphonate (4·31 g.) and 3 : 5-di-iodo-*p*-cresol (7·2 g.) in pyridine (20 ml.) by the method described above for the benzaldehyde analogue. The *diphenyl ether* (1·4 g., 34%) separated from aqueous acetic acid as pale yellow prisms, m. p. 140—141° (Found: N, 6·8; I, 31·3. $C_{14}H_{11}O_5N_2I$ requires N, 6·8; I, 30·7%).

Methyl 3-*Iodo*-4-(2′ : 6′-*dinitro*-4′-*carbomethoxyphenoxy*)*benzoate*.—Methyl 4-chloro-3 : 5-dinitrobenzoate (1·30 g.) and pyridine (6·5 ml.) were heated together on the steam-bath for 20 minutes. Methyl 3 : 5-di-iodo-4-hydroxybenzoate (4·04 g.) was added and the solution was heated on the steam-bath for a further 2 hours. The *diphenyl ether* (1·1 g., 44%), purified by passage of its acetone solution through an alumina column, crystallised from aqueous acetic acid in prisms, m. p. 159—160° (Found: N, 5·6; I, 25·4. $C_{16}H_{11}O_9N_2I$ requires N, 5·6; I, 25·3%).

2 : 6-*Dinitro*-4-*methoxyphenyl Toluene*-p-*sulphonate*.—A mixture of 2 : 6-dinitro-4-methoxyphenol (Weselsky and Benedikt, *Monatsh.*, 1881, **2**, 369) (1·07 g.), toluene-*p*-sulphonyl chloride (1·0 g.), and water (10 ml.) was heated on the steam-bath with stirring while sodium carbonate (1·06 g.) was added in small portions. Since the deep-red colour persisted, further quantities of toluene-*p*-sulphonyl chloride and sodium carbonate were added until the alkaline solution was only faintly red. The solid was filtered off, and washed well with warm sodium carbonate solution and then with water. The *toluene*-p-*sulphonate* (1·75 g., 96%) melted at 140—141° after crystallisation from ethanol (Found: N, 7·9; S, 9·1. $C_{14}H_{12}O_9N_2S$ requires N, 7·65; S, 8·75%).

1-(2 : 6-*Dinitro*-4-*methoxyphenyl*)*pyridinium Toluene*-p-*sulphonate*.—The foregoing ester (1 g.) in pyridine (5 ml.) was kept overnight at room temperature and ether was added to precipitate the quaternary *salt* (0·9 g., 74%) which crystallised as needles from ethanol–ether and melted at 199—201° (Found: C, 51·0; H, 3·8; S, 7·3. $C_{19}H_{17}O_9N_3S$ requires C, 51·0; H, 3·8; S, 7·2%).

2-Iodo-2′ : 6′-dinitro-4′-methoxy-4-methyldiphenyl Ether.—The foregoing quaternary salt (4 g.) in pyridine (25 ml.) was treated with 3 : 5-di-iodo-*p*-cresol (8 g.), and the solution was heated on the steam-bath for 2 hours. The *diphenyl ether*, isolated in the usual way, was a light yellow solid (0·4 g.) which melted at 161—163° after crystallisation from aqueous acetic acid (Found : N, 6·2; I, 30·0. $C_{14}H_{11}O_6N_2I$ requires N, 6·5; I, 29·5%).

Methyl 3 : 5-*Dinitro*-4-(3 : 5-*di-iodo*-4-*methylphenoxy*)*benzoate*.—Methyl 4-chloro-3 : 5-dinitrobenzoate (2·6 g.), 3 : 5-di-iodo-*p*-cresol (3·6 g.), potassium carbonate (2·8 g.), and methyl ethyl ketone (10 ml.) were boiled together under reflux for 1 hour. The solution was filtered and the filtrate evaporated leaving a dark red oil which was dissolved in chloroform. The solution was washed with N-sodium hydroxide and then with water, dried ($MgSO_4$), and evaporated. The residual yellow solid was washed with a little ether and crystallised from aqueous acetic acid, the *diphenyl ether* (3·0 g., 51%) being obtained as pale yellow plates, m. p. 170—172° (Found : N, 4·8; I, 43·9. $C_{15}H_{10}O_7N_2I_2$ requires N, 4·8; I, 43·5%).

After heating this compound (2·5 g.) with morpholine (10 ml.) on the steam-bath for 2 hours it was possible to isolate, from the alkali-soluble fraction, a small quantity of 3 : 5-di-iodo-*p*-cresol, m. p. and mixed m. p. 60—62°.

3 : 5-*Di-iodo*-4-*allyloxy*-N-*acetyl*-DL-*phenylalanine*.—3 : 5-Di-iodo-*N*-acetyl-DL-tyrosine (4·49 g.), dissolved in absolute ethanol (80 ml.) containing sodium (0·49 g., 2 equivs.), was boiled under reflux with allyl chloride (6 ml.) for 5 hours and then treated with a further 6 ml. of allyl chloride for 2 hours. After 48 hours at room temperature the reaction mixture was concentrated under reduced pressure, diluted with water, acidified, and extracted with ether. The ethereal extract was washed with water and dried. Evaporation of the ether left the *allyl ether* (4 g.) which crystallised from aqueous alcohol as needles, m. p. 176·5° (Found : C, 32·9; H, 3·1; N, 2·6; I, 49·0. $C_{14}H_{15}O_4NI_2$ requires C, 32·6; H, 2·9; N, 2·7; I, 49·3%).

3 : 5-*Di-iodo*-4-(cyclo*hex*-2-*enyloxy*)-N-*acetyl*-DL-*phenylalanine*.—3 : 5-Di-iodo-*N*-acetyl-DL-tyrosine (4·75 g.), 3-bromo*cyclo*hexene (2 g.), potassium carbonate (4 g.), and methyl ethyl ketone (25 ml.) were boiled together under reflux for 16 hours. The solution was filtered and evaporated to dryness under reduced pressure. The residue was treated with water and a little 2N-sodium hydroxide to effect complete dissolution of the black gum. The aqueous solution was washed with ether, covered with fresh ether, and acidified with 2N-hydrochloric acid. Evaporation of the dried ethereal solution yielded a gum (3·7 g.), which was dissolved in acetone (*ca.* 20 ml.). The acetone solution was filtered from a little insoluble product, treated with charcoal, and then diluted with light petroleum (b. p. 60—80°). Slow evaporation of this solution at room temperature yielded the desired *ether*, which crystallised from aqueous acetone as a colourless powder, m. p. 147° (decomp.) (Found : C, 36·4; H, 3·4; N, 2·5; I, 46·6. $C_{17}H_{19}O_4NI_2$ requires C, 36·8; H, 3·4; N, 2·5; I, 45·8%).

Methyl 3 : 5-*Di-iodo*-4-(cyclo*hex*-2-*enyloxy*)*benzoate*.—Methyl 3 : 5-di-iodo-4-hydroxybenzoate (3·0 g.), 3-bromo*cyclo*hexene (1·7 g.), potassium carbonate (4·0 g.), and methyl ethyl ketone (20 ml.) were boiled together under reflux for 20 hours. After concentration the resulting gum was washed with water and extracted with ether. The extract was washed with 2N-sodium hydroxide and then with water, dried ($MgSO_4$), and concentrated to yield an oil (3·1 g., 86%) which slowly crystallised. This *ether* crystallised from ethanol or light petroleum (b. p. 60—80°) as clusters of colourless needles, m. p. 91°. It could be sublimed rapidly at 150°/0·0005 mm. (Found : C, 34·8; H, 3·2; I, 53·75. $C_{14}H_{14}O_3I_2$ requires C, 34·7; H, 2·9; I, 52·5%).

Although the ether seemed stable at temperatures just above its melting point, slow gas evolution occurred at *ca.* 190°, becoming more rapid at *ca.* 220°. After 2 hours in boiling xylene 70% of the ether was split to methyl 3 : 5-di-iodo-4-hydroxybenzoate, and 50% of the ether was destroyed by similar treatment lasting only 30 minutes.

The ester grouping of the ether was hydrolysed by heating the compound with 2N-sodium hydroxide on the steam-bath for 90 minutes. This yielded 3 : 5-*di-iodo*-4-(cyclo*hex*-2-*enyloxy*)*benzoic acid* which crystallised from benzene as rosettes or soft white needles. The melting point varied according to the rate of heating but when placed in a bath at 150°, the compound appeared to lose solvent at 160—165° and melted sharply at 238° (decomp.) with evolution of iodine (Found : C, 33·9; H, 2·6. $C_{13}H_{12}O_3I_2$ requires C, 33·2; H, 2·55%).

3 : 5-*Di-iodo*-4-(cyclo*hex*-2-*enyloxy*)*benzaldehyde*.—This ether was prepared in 76% yield by treatment of 3 : 5-di-iodo-4-hydroxybenzaldehyde (19·5 g.) with 3-bromo*cyclo*hexene (11·0 g.) in the presence of potassium carbonate (19·0 g.) in methyl ethyl ketone (120 ml.) in the usual way. Several attempts to purify it by distillation at pressures down to 0·0005 mm. resulted in rapid decomposition with loss of iodine. The ether, an alkali-insoluble syrup, was characterised as its orange-coloured 2 : 4-*dinitrophenylhydrazone*, m. p. 258—260° (decomp.) (Found : N, 8·2. $C_{19}H_{14}O_6N_4I_2$ requires N, 8·8%).

The stability of the ether in boiling xylene was of the same order as that of the corresponding benzoate.

3 : 5-*Di-iodo*-4-(cyclo*hex*-2-*enyloxy*)*toluene*.—3 : 5-Di-iodo-*p*-cresol (5 g.) in methyl ethyl ketone (30 ml.) was boiled under reflux with 3-bromo*cyclo*hexene (2·9 g.) and potassium carbonate (5 g.) for 20 hours. The reaction mixture was worked up in the usual manner to yield the *ether* as a crude oil (6·0 g.) which could be distilled rapidly at 140°/0·00005 mm. as a very pale yellow oil (Found : C, 35·3; H, 3·3; I, 59·4. $C_{13}H_{14}OI_2$ requires C, 35·45; H, 3·2; I, 57·7%).

This ether was markedly more stable to heat than the related aldehyde and ester. Thus, in boiling xylene, iodine was liberated much more slowly and even after 3½ hours 25% of the material was recovered as an alkali-insoluble, non-volatile oil.

Reaction of Methyl 3 : 5-*Di-iodo*-4-(cyclo*hex*-2-*enyloxy*)*benzoate with Selenium Dioxide*.—The ether (2·0 g.), selenium dioxide (1·1 g.), acetic acid (10 ml.), and water (0·5 ml.) were heated together on the steam-bath for 15 hours. During this period much iodine was liberated and an insoluble solid separated.

This solid (0·85 g.) was very insoluble in the usual organic solvents, but dissolved in aqueous sodium hydrogen carbonate, from which solution it was precipitated unchanged by acidification. Before analysis, it was washed successively with aqueous sodium pyrosulphite, aqueous potassium cyanide, acetone, and ethanol. It melted at 290° (decomp.) and contained selenium (Found: C, 36·3; H, 2·7; I, 27·9%). The same compound resulted when aqueous ethanol or aqueous dioxan was used as solvent for the oxidation.

Methyl **3**:5-*Di-iodo*-4-(4-*acetoxy*cyclo*hex*-2-*enyloxy*)*benzoate*.—A mixture of methyl **3**:5-di-iodo-4-hydroxybenzoate (5 g.), 3-bromo-6-acetoxy*cyclo*hexene (Ziegler *et al.*, *Annalen*, 1942, **551**, 80) (3·75 g.), potassium carbonate (5 g.), and methyl ethyl ketone (25 ml.) was boiled under reflux for 21 hours. The reaction mixture was filtered and the filtrate evaporated to dryness under reduced pressure. The residue was treated with ether and water, and some insoluble material was filtered off. The ethereal layer from the filtrate was washed with alkali and water in the usual way to yield a crude oil after evaporation. Distillation of the crude ether at 130—140°/0·00005 mm. yielded a solid by-product which crystallised from aqueous methyl alcohol as buff-coloured needles, m. p. 254° (decomp.), which were soluble in 2*N*-sodium hydroxide and saturated aqueous sodium hydrogen carbonate; the material was not examined further.

The required *ether* distilled at 220°/0·00005 mm. as a yellow glass (Found: C, 35·5; H, 3·0; I, 47·6. $C_{16}H_{14}O_5I_2$ requires C, 35·4; H, 2·95; I, 46·9%).

The acetoxy*cyclo*hexenyl ether (1·1 g.) was hydrolysed by heating it for 1 hour on the steam-bath with a mixture of 2*N*-sodium hydroxide (10 ml.) and ethanol (15 ml.). The resulting solution was treated with charcoal, filtered, washed with ether, and then acidified, to yield a white precipitate which crystallised from aqueous methanol as feathery needles, m. p. 257° (decomp.), not depressed on admixture with an authentic specimen of **3**:5-di-iodo-4-hydroxybenzoic acid.

The acetoxy*cyclo*hexenyl ether proved to be much more stable than the corresponding *cyclo*hexenyl ether, 80% being recovered after 1 hour's heating in xylene.

3:5-*Di-iodo*-4-(4-*acetoxy*cyclo*hex*-2-*enyloxy*)*toluene*.—A mixture of **3**:5-di-iodo-*p*-cresol (4·9 g.), 3-bromo-6-acetoxy*cyclo*hexene (3·7 g.), potassium carbonate (5 g.), and methyl ethyl ketone (25 ml.) was boiled under reflux for 21 hours. Worked up in the usual manner, the required *ether* was obtained as a crude oil (5·35 g., 79%) which could be distilled as a pale yellow syrup at 140°/0·001 mm. (Found: C, 36·3; H, 3·0; I, 51·1. $C_{15}H_{16}O_3I_2$ requires C, 36·15; H, 3·2; I, 51·0%).

After boiling of a xylene solution of the ether for 2 hours, 93% of the ether was recovered unchanged.

Dihydroresorcinol.—The method of Birch (*J.*, 1947, 102) was used, but in the last stage the liquor from which the first crop of dihydroresorcinol had separated was evaporated to a gum and subjected again to the treatment with hydrochloric acid to complete the decomposition of the dimethyl compound. In this way an overall yield of 40% was achieved. The compound, in ethanol solution, had $E^{1\%}_{1\,cm.}$ = 2530 at $\lambda_{max.}$ 282 mμ.; in the presence of sodium ethoxide (1 equiv.) this became $E^{1\%}_{1\,cm.}$ = 1680 at $\lambda_{max.}$ 255 mμ.

3:5-*Di-iodo*-4-(3-*keto*cyclo*hex*-1-*enyloxy*)*toluene*.—Crude 3-chloro*cyclo*hex-2-enone (Crossley and Haas, *J.*, 1903, 494) (4·72 g.) was dissolved in methyl ethyl ketone (50 ml.) containing **3**:5-di-iodo-*p*-cresol (13·1 g.) and anhydrous potassium carbonate (18 g.). The solution was boiled under reflux for 24 hours, and the solid was filtered off. The filtrate was evaporated to small bulk and extracted with ether. The extract was washed successively with 2*N*-sodium hydroxide (to remove unchanged **3**:5-di-iodo-*p*-cresol), acid, and water, dried ($MgSO_4$), and evaporated to an oil (9·66 g.). This was extracted with a little cold ethanol, giving (*a*) a soluble unidentified fraction (6·38 g.) most of which boiled at 90°/3 × 10^{-4} mm. and (*b*) an insoluble crystalline solid (3·28 g.), separating from ethanol as large white prisms, which melted at 152—153° and evolved iodine at 280°. This was **3**:5-*di-iodo*-4-(3-*keto*cyclo*hex*-1-*enyloxy*)*toluene* (Found: C, 34·6; H, 2·6; I, 55·9%; *M*, 429. $C_{13}H_{12}O_2I_2$ requires C, 34·4; H, 2·6; I, 55·9%; *M*, 454). It gave no colour with ferric chloride in aqueous ethanol. In warm ethanol it yielded a **2**:4-*dinitrophenylhydrazone*, as very small red crystals, m. p. 193°, giving no colour with ferric chloride or acid potassium chromate solution (Found: C, 36·3; H, 2·5; N, 8·8; I, 40·1. $C_{19}H_{16}O_6N_4I_2$ requires C, 36·0; H, 2·5; N, 8·8; I, 40·1%). It was recovered unchanged after being heated for 24 hours on the steam-bath with acetic anhydride, or after 2 hours in boiling xylene, with or without a palladised charcoal catalyst.

Bromination and Dehydrobromination of **3**:5-*Di-iodo*-4-(3-*keto*cyclo*hex*-1-*enyloxy*)*toluene*.—A solution of the ether (2·27 g.) and *N*-bromosuccinimide (0·89 g.) in carbon tetrachloride (25 ml.) was boiled under reflux for 8 hours. The resulting succinimide (0·41 g.) was filtered off, and the filtrate was concentrated to an oil, setting to a semicrystalline mass. The bromo-ketone yielded a **2**:4-*dinitrophenylhydrazone*, which crystallised from ethanol as very small red crystals, m. p. 140—145° (Found: N, 8·4. $C_{19}H_{15}O_6N_4BrI_2$ requires N, 7·9%).

A solution of the crude bromo-compound in **2**:**4**:6-collidine (10 ml.) was boiled under reflux for 70 minutes. The cooled solution was treated with ether, the insoluble part being a water-soluble, brown solid, presumably collidine hydrobromide. The solution was washed with acid (slight excess) and water, dried ($MgSO_4$), and concentrated to a brown oil, which could be crystallised from ether or alcohol as a white solid, m. p. 148—149° (1·9 g.), insoluble in alkali. This had the composition of a **3**:5-*di-iodo*-4-(3-*keto*cyclo*hexadienyloxy*)*toluene* (Found: I, 55·9. $C_{13}H_{10}O_2I_2$ requires I, 56·3%). It yielded a **2**:4-*dinitrophenylhydrazone* which separated from ethanol–ethyl acetate as red needles, m. p. 173—175° (Found: N, 8·7; I, 39·3. $C_{19}H_{14}O_6N_4I_2$ requires N, 8·9; I, 40·2%).

The crude dehydrobromination product was left at room temperature for 5 hours in acetic anhydride (30 ml.) containing sulphuric acid (5 drops). The solution was poured into ice–water, whereupon **2**:6-*di-iodo*-3′-*acetoxy*-4-*methyldiphenyl ether* (1·9 g., 77%) separated as a solid which crystallised from

aqueous ethanol as a feathery mass, m. p. 110°, not depressed on admixture with a specimen prepared as described below (Found : I, 51·1. $C_{19}H_{15}O_3I_3$ requires I, 51·4%).

2 : 6-*Dinitro*-3'-*hydroxy*-4-*methyldiphenyl Ether*.—**3** : 5-Dinitro-*p*-tolyl toluene-*p*-sulphonate (35 g.) was heated in boiling anhydrous pyridine (250 ml.) with resorcinol (110 g.) for 1 hour. The pyridine was removed under reduced pressure. The residue was extracted with chloroform and the extract washed with dilute hydrochloric acid. Free phenolic material was extracted into ice-cold N-sodium hydroxide, which was run immediately into an excess of hydrochloric acid, thus precipitating an oil. The chloroform layer was washed with acid and then water, dried ($MgSO_4$), and concentrated to a residue (7·1 g.) which crystallised from glacial acetic acid as slightly yellow needles of *m*-*di*-(2 : 6-*dinitro*-4-*methylphenoxy*)-*benzene*, m. p. 217° (Found : C, 50·7; H, 3·1; N, 12·3. $C_{26}H_{18}O_{10}N_4$ requires C, 51·0; H, 3·0; N, 11·9%).

The phenolic fraction was extracted into chloroform and washed with ice-cold 2N-sodium carbonate, then with dilute hydrochloric acid, and finally with water. The dried ($MgSO_4$) solution was evaporated to a gum (26 g.) which, on distillation at 5 × 10^{-4} mm., yielded only a small sublimate of **3** : 5-dinitro-*p*-cresol, m. p. 82°, identified by comparison with an authentic specimen. The gum (25 g.) was therefore boiled under reflux with acetic anhydride (90 ml.), containing fused sodium acetate (3 g.), for 2 hours. The sodium acetate was removed by filtration, and the solvent was removed from the filtrate by co-distillation under reduced pressure with xylene. The residual **2** : 6-*dinitro*-3'-*acetoxy*-4-*methyldiphenyl ether* crystallised from aqueous ethanol as white spikes (10 g.), m. p. 138° (Found : C, 54·5; H, 3·85; N, 8·2. $C_{16}H_{12}O_7N_2$ requires C, 54·2; H, 3·6; N, 8·4%).

The above acetoxy-compound (1·0 g.) was boiled under reflux with a mixture of ethanol (10 ml.) and concentrated hydrochloric acid (10 ml.) for 2 hours. The solvents were removed under reduced pressure and the residue was extracted into ether. The extract was washed with water, dried ($MgSO_4$), and evaporated to an oil (0·9 g.) which could be crystallised at −30° from aqueous ethanol, but was better purified by distillation at 143°/10^{-4} mm.; **3** : 5-*dinitro*-3'-*hydroxy*-4-*methyldiphenyl ether* collected as an amber-coloured gum (Found : C, 53·9; H, 3·7; N, 9·9. $C_{19}H_{16}O_5N_2$ requires C, 53·8; H, 3·4; N, 9·7%).

2 : 6-*Di-iodo*-3'-*acetoxy*-4-*methyldiphenyl Ether*.—The foregoing acetoxy-ether (3·32 g.) in acetic acid (100 ml.) was shaken with palladised charcoal (10%; 1 g.) in the presence of hydrogen at atmospheric pressure and temperature. The diamine obtained by evaporation of the filtered solution was unstable in air and light, as were the hydrochloride, sulphate, picrate, and *m*-nitrobenzenesulphonate. The base was characterised by repeating the hydrogenation in the presence of acetic anhydride (3 ml.), removing the catalysts and solvent in the normal way, and crystallising the residual gum from ethanol; **2** : 6-*bis-acetamido*-3'-*acetoxy*-4-*methyldiphenyl ether* separated as white needles (2·8 g.), m. p. 195—196° (Found : C, 63·7; H, 5·6; N, 7·95. $C_{19}H_{20}O_5N_2$ requires C, 64·0; H, 5·6; N, 7·9%).

For the tetrazotisation, the freshly hydrogenated acetic acid solution of the diamine was concentrated under reduced pressure to small bulk (*ca.* 20 ml.) and added dropwise to a stirred ice-cold solution of sodium nitrite (1·7 g.) in concentrated sulphuric acid (25 ml.). The tetrazonium solution was stirred for a further hour at 0°, crystalline material separating. This slurry was then added slowly to an ice-cold solution of sodium iodide (4·5 g.) and iodine (3·7 g.) in water (70 ml.). The mixture was stirred overnight and the black tar was washed several times with boiling 10% aqueous sodium iodide. The pulverised product was dissolved in acetone and filtered on to an alumina pad, wet with light petroleum. An orange-brown zone, rapidly eluted with light petroleum, was collected. **3** : 5-*Di-iodo*-3'-*acetoxy*-4-*methyldiphenyl ether* (1·4 g., 28%) crystallised from ethanol as feathery white clusters, m. p. 111° (Found : C, 36·5; H, 2·7; I, 51·0. Calc. for $C_{15}H_{12}O_3I_2$: C, 36·5; H, 2·45; I, 51·4%).

This compound (1 g.) was hydrolysed in boiling ethanol (20 ml.) containing 10N-sodium hydroxide (10 ml.) for 90 minutes. The cooled solution was poured into ice-cold hydrochloric acid, and the mixture was extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated to an oil (0·7 g.) distilling at 160°/5 × 10^{-4} mm., consisting of **3** : 5-*di-iodo*-3'-*hydroxy*-4-*methyldiphenyl ether* (Found : C, 34·6; H, 2·5; I, 57·2. $C_{13}H_{10}O_2I_2$ requires C, 34·5; H, 2·2; I, 56·1%).

4-*Bromocyclohex*-2-*enone*.—*cyclo*Hex-2-enone (4·8 g.), *N*-bromosuccinimide (8·9 g.), benzoyl peroxide (100 mg.), and carbon tetrachloride (100 ml.) were boiled together under reflux for 45 minutes. The mixture was cooled to 0°, filtered, and evaporated to dryness under reduced pressure. The residual oil, which was extremely unstable, was used immediately, without further purification.

Reaction of 4-*Bromocyclohex*-2-*enone with* **3** : 5-*Di-iodo*-p-*cresol*.—A mixture of crude 4-bromo*cyclo*hex-2-enone, prepared as described above, with **3** : 5-di-iodo-*p*-cresol (18 g.), anhydrous potassium carbonate (20 g.), and methyl ethyl ketone was boiled under reflux for 18 hours. The mixture was then poured into water and extracted with ether, and the extract washed with dilute sodium hydroxide solution and then dilute hydrochloric acid. The dried ethereal extract on evaporation yielded an oil which, on distillation at very low pressure, gave two main fractions. The first, distilling at 83—85°/10^{-4} mm., has not been identified, but the second, distilling at 120—125°/10^{-4} mm., consisted of the ether contaminated with **3** : 5-di-iodo-*p*-cresol. This latter was removed by alkali-washing, and the ether was analysed as its **2** : 4-*dinitrophenylhydrazone*, which melted at 185° after crystallisation from benzene–ether (Found : N, 8·8; I, 39·9. $C_{19}H_{14}O_5N_4I_2$ requires N, 8·85; I, 40·0%). The yield was 10%.

The authors thank Mr. L. J. Wyman and Mr. G. J. Waller for their assistance in the experimental work.

RESEARCH DIVISION, GLAXO LABORATORIES, LTD.,
GREENFORD, MIDDLESEX.

[*Received, June 5th,* 1950.]

548. *The Kinetics of Halogen Addition to Unsaturated Compounds. Part XIX. The αβ-Ethylenic Nitriles.*

By D. A. Evans and P. W. Robertson.

The relative rates of electrophilic chlorine addition in acetic acid solution are in the order, $CHPh{:}CH{\cdot}CN > CHMe{:}CH{\cdot}CN > CH_2{:}CH{\cdot}CN$, and $CHPh{:}CH{\cdot}CN > CHPh{:}CPh{\cdot}CN$, and with respect to other deactivating groups there is the series, $CHPh{:}CHBr > CHPh{:}CH{\cdot}CO_2H > CHPh{:}CH{\cdot}CHO > CHPh{:}CH{\cdot}CN \simeq CHPh{:}CH{\cdot}NO_2$. The compounds $CHR{:}CH{\cdot}CN$ further add bromine by the nucleophilic acid-catalysed mechanism, and the relative rates with HBr_3 are $CHMe{:}CH{\cdot}CN > CHPh{:}CH{\cdot}CN$, and $CHPh{:}CH{\cdot}CHO > CHPh{:}CH{\cdot}CN > CHPh{:}CH{\cdot}NO_2$.

There appears to be no record of kinetic measurements of halogen addition to the acrylonitriles, except 1-phenylcinnamonitrile. This compound adds bromine in carbon tetrachloride solution extremely slowly in the dark, but in light the addition proceeds reversibly, giving an equilibrium which is independent of the intensity of the illumination (Berthoud and Nicolet, *J. Chim. physique*, **1928**, **40**). This reaction is of interest in that very few examples of reversible bromine addition at ordinary temperatures are known, and a reference to the influence of temperature on the equilibrium is made on p. 2835. It is, however, more especially the nature of thermal halogen addition which is the subject of this series of investigations. The cyanide group, attached to an ethylene carbon atom, by virtue of its considerable inductive and tautomeric effects ($-I$, $-T$, in Ingold's nomenclature) should have a powerful deactivating influence on electrophilic reactivity. This is revealed in the slow rates of chlorine addition in acetic acid solution at 25° to cinnamo-, crotono-, and acrylo-nitriles:

$CHPh{:}CH{\cdot}CN$	$CHMe{:}CH{\cdot}CN$	$CH_2{:}CH{\cdot}CN$ *
$k_2 = 0{\cdot}022$	$k_2 = 0{\cdot}0017$	$k_2 \sim 0{\cdot}0001$

* In presence of sodium acetate to prevent polymerisation.

These rates are in the same order as those for the corresponding acids, and smaller by a factor of about 200. The deactivating influence of the cyano-group on chlorine addition, in comparison with certain other groups, is shown by reference to $CHPh{:}CHBr$ ($k_2 = 30$) and $CHPh{:}CH{\cdot}NO_2$ ($k_2 = 0{\cdot}020$). Whereas Br reduces the rate of chlorination of $CHPh{:}CHBr$ by an inductive effect only, CN has a larger dipole moment and acts both by its inductive and by its mesomeric and electromeric effects, as seen from the large difference in rates between the bromide and the nitrile. The cyano- and nitro-groups have similar dipole moments, but in certain reactions behave as if the combined mesomeric and electromeric effects of the nitro-group were superior, as, *e.g.*, in the reactions of the *p*-bromonitrobenzene and *p*-bromocyano-benzene with alkali (Barnett and Levett, *J. Amer. Chem. Soc.*, **1948**, **70**, 2778).

Whereas a single phenyl group attached to the ethylene system has an activating effect on halogen addition ($+T$), another phenyl on the second ethylene carbon acts reversely ($-T$), as discussed by Ingold and Ingold (*J.*, **1931**, 2354) and experimentally confirmed in Part X of this series for the compounds $CHPh{:}CH_2$ and $CHPh{:}CHPh$ (*J.*, **1947**, 628). A similar effect is to be expected in the compounds now under consideration, and rates of chlorine addition to cinnamo-nitrile and its 1-phenyl derivative are now given. The measurements, owing to the low reactivities in acetic acid, are made in 25% aqueous acetic acid (at 25°), and the arrow indicates the point of electrophilic attack:

$CHPh{=}\overset{\curvearrowright}{C}H{\cdot}CN$ $k_2 = 2{\cdot}0$ $\qquad$ $CHPh{=}\overset{\curvearrowright}{C}Ph{\cdot}CN$ $k_2 = 0{\cdot}27$

The reactions so far considered have been electrophilic in character. The acid-catalysed nucleophilic mode of halogen addition has been demonstrated for compounds containing $-T$ groups, such as CHO or NO_2, and the CN group similarly should be capable of causing this type of reaction, as it is possible to form compounds of the type $\overset{\oplus}{C}HR{\cdot}CH{:}C{:}NH$ by addition of a proton.

Perchloric acid in acetic acid solution was found to cause marked catalysis of bromine addition, as indicated by the initial rates for $CHPh{:}CH{\cdot}CN$ (reactants M/40) at 25°:

$$k_2(NaOAc,\ M/40) < 0{\cdot}0001 \quad k_2(HClO_4,\ M/40) > 0{\cdot}26$$

The rates for this compound with perchloric acid were not perfectly reproducible and moreover decreased considerably after the initial absorption, a behaviour apparently due to concomitant polymerisation. With excess of hydrogen bromide, however, *i.e.*, with $Br_3^{\ominus}$ as the nucleophilic

reagent, the bimolecular coefficients remained constant over the greater part of the addition, indicating the absence of a disturbing side reaction. With crotononitrile, on the other hand, there was a slight falling off in rate even when HBr_3 was the reagent, and this became more considerable for acrylonitrile. The following values of the initial rate were recorded in acetic acid at 25°, M/40-reactants, with M/5-HBr:

	CHPh:CH·CN	CHMe:CH·CN	CH_2:CH·CN
k_2, HBr_3 ($x = 20$)	4·1	5·7	~0·72

The rate for CHPh:CH·CN may be compared with the rates obtained under similar conditions with other compounds also containing strongly electron-attracting groups, *viz.*, CHPh:CH·CHO ($k_2 \sim 300$) and CHPh:CH·NO_2 ($k_2 = 0{\cdot}83$). Such nucleophilic rates, as pointed out in previous communications, being dependent on opposing electronic requirements, are not necessarily in the reverse order of the electrophilic rates of the compounds. It may be predicted, however, that when the electrophilic rate of chlorine addition to a compound is very low, owing to the influence of a group with a large $-T$ effect, the rate of bromine addition in the presence of hydrogen bromide will be considerably greater [*e.g.*, for CH_2:CH·CN, $k_2(Cl_2) \sim 0{\cdot}0001$, $k_2(HBr_3) \sim 0{\cdot}7$].

In earlier communications (*loc. cit.*) we have proposed the theory that, for compounds containing CHO and NO_2 groups, the reaction may proceed by way of 1 : 4-addition of HBr_3.

For such compounds, a one-stage process of this type is sterically possible (I), but for the αβ-unsaturated nitriles the linearity of the CH:C:N⊕ system keeps the attacked centres at a greater distance apart (II), and it seems more likely, therefore, that the addition process involves attack by H⊕ and Br_3⊖ in separate stages of the reaction, as is formulated in general terms in the following paper.

Experimental.

The following compounds were used in this investigation: cinnamonitrile, b. p. 255—257°/760 mm.; crotononitrile, b. p. 118—119°/757 mm.; acrylonitrile (Light and Co.), b. p. 78°/757 mm.; 1-phenylcinnamonitrile, m. p. 86°. The first three nitriles were purified by distillation immediately before use, as they tend to polymerise. The reactions were carried out in duplicate in tightly stoppered bottles in the dark; for some of the slower reactions, sealed tubes were used. The following are details of a typical rate determination:

M/40-PhCH:CH·CN + M/40-Br_2 + M/5-HBr in acetic acid at 25°;
1-ml. samples titrated with N/80-sodium thiosulphate.

Time (mins.) ...	0	3	6	9	12	16·5	0	1·2	3·2	7	10	20
Titre (ml.)	3·99	3·05	2·45	2·09	1·81	1·43	3·99	3·57	3·05	2·29	2·00	1·23

All the points lay on a smooth curve which gave constant k_2 values.

x (% addition)	10	20	30	40	50	60
k_2	4·1	4·1	4·1	4·1	4·05	4·1

Additional results are given as times (minutes) for $x = 20\%$ halogen addition, at 25°, in acetic acid, unless otherwise indicated:

M/40-CHPh:CH·CN + M/40-Br_2 + M/20-$HClO_4$, $t = 38$; M/40-CHPh:CH·CN + M/40-Cl_2, $t = 465$; M/80-CHPh:CH·CN + M/80-Cl_2 in acetic acid + 25% water, $t = 10$; M/40-CHMe:CH·CN + M/40-Cl_2, $t = 5640$; M/40-CHMe:CH·CN + M/40-Br_2 + M/5-HBr, $t = 1{\cdot}7$; M/40-CH_2:CH·CN + M/40-Br_2 + M/5-HBr, $t = 12{\cdot}5$; M/4-CH_2:CH·CN, + M/40-Cl_2 + M/40-NaOAc, $t = 13220$; M/40-CHPh:CPh·CN + M/40-Cl_2 + M/40-NaOAc, $t = 7130$; M/40-CHPh:CPh·CN + M/40-Cl_2, in acetic acid + 25% water, $t = 37$.

The influence of temperature on the equilibrium between 1-phenylcinnamonitrile and bromine was examined qualitatively. Sealed tubes of reactants, M/40 in carbon tetrachloride solution, were illuminated at 25° until attainment of equilibrium. One of these tubes was then illuminated at 0°, and a second at 50°, and kept at these temperatures for some days. The change in colour of the solutions was easily evident, the dissociation to yield bromine being greatest at 50° and least at 0°. On re-illumination at 25°, all the solutions regained the same tint, indicating the absence of concomitant polymerisation under these experimental conditions.

Victoria University College, Wellington,
New Zealand.

[*Received, June 8th*, 1950.]

549. *The Kinetics of Halogen Addition to Unsaturated Compounds. Part XX. αβ-Unsaturated Sulphones.*

By I. R. C. McDonald, R. M. Milburn, and P. W. Robertson.

The strong electron-attracting power ($-I$) of the $SO_2{\cdot}CH_3$ and SO_2Cl groups is shown by the sequence of relative rates of electrophilic chlorine addition in acetic acid, *viz.*, $CH_2{:}CH{\cdot}CO_2Et > CH_2{:}CH{\cdot}SO_2Me$ and $CHPh{:}CH{\cdot}COCl > CHPh{:}CH{\cdot}NO_2 > CHPh{:}CH{\cdot}SO_2Cl$. Bromine addition to $CH_2{:}CH{\cdot}SO_2Me$ and to $CH_2{:}CH{\cdot}SO_2Bu$ is more rapid than chlorine addition, and is catalysed considerably by lithium chloride, and more so by lithium bromide. These reactions with bromine differ from the corresponding reactions of αβ-unsaturated aldehydes and similar compounds, in that the former are little catalysed by acids, hydrogen bromide being less effective as a catalyst than lithium bromide. The kinetics of halogenation of $CH_2{:}CH{\cdot}SO_2H$, $CH_2{:}CH{\cdot}SO_2Na$, and $CHPh{:}CH{\cdot}SO_2Na$ are complicated by the ionisation of these compounds in acetic acid.

There do not appear to have been any previous rate measurements of halogen addition to the αβ-unsaturated sulphones, or related compounds containing a sulphonyl group. In connection with the general development of the theory of halogen addition, it was demonstrated by Ingold and Smith (*J.*, **1931**, 2749) that in the action of iodine chloride on ethylenesulphonic acid, the electrophilic attack was on the α-carbon atom of the ethylene system, the product being the compound $CH_2Cl{\cdot}SO_2H$. Similarly, ethylenesulphonic acid on bromination in water forms the α-bromo-derivative (cf. Suter, "Organic Chemistry of Sulphur," p. 171). The occurrence of substitution in preference to addition when the attack is on a negative ion was also found by Bardwell and Rondestvedt (*J. Amer. Chem. Soc.*, **1948**, **70**, 2429) for the action of bromine on the salt $CHPh{:}CH{\cdot}SO_3Na$ in aqueous solution; on the other hand, they noted addition of bromine to the un-ionised compounds, $CHPh{:}CH{\cdot}SO_2Et$ and $CHPh{:}CH{\cdot}SO_2NH_2$, in non-aqueous solvents.

Rates of reaction of chlorine and of bromine in acetic acid at 25° with various sulphones and sulphonyl derivatives have been measured, and are recorded as bimolecular coefficients (k_2, l. g.-mol.$^{-1}$ min.$^{-1}$).

Electrophilic Chlorine Addition.—The following rates of chlorine disappearance, whether due to addition or to substitution, are for electrophilic reactions, as is shown by the effect of structure on reactivity:

	$CH_2{:}CH{\cdot}CO_2Et$	$CH_2{:}CH{\cdot}SO_2Me$	$CH_2{:}CH{\cdot}SO_2H$	$CH_2{:}CH{\cdot}SO_2Na$
k_2	0·056	0·0001	0·11	0·73
	$CHPh{:}CH{\cdot}COCl$	$CHPh{:}CH{\cdot}NO_2$	$CHPh{:}CH{\cdot}SO_2Cl$	
k_2	5·7	0·020	0·006	

Because of the great electron attraction of the SO_2 group, the neutral compound methyl vinyl sulphone is extremely unreactive by this mechanism, reacting with chlorine more slowly than ethyl acrylate by a factor of about 600. The relatively high rate for ethylenesulphonic acid is due to the fact that this compound is ionised in acetic acid, having a conductivity between those of sulphuric and perchloric acid. The reaction is, therefore, substantially that of the anion, and the high electrophilic reactivity of unsaturated anions, previously demonstrated in aqueous solution (*J.*, **1937**, 335), is now shown for acetic acid as solvent. The salt sodium ethylenesulphonate, which, owing to its conductivity being higher than that of the acid, is expected to be more dissociated, correspondingly has a higher electrophilic rate of chlorination. The SO_2Cl group is even more powerfully deactivating than SO_2Me, being considerably greater in its effect on the rate than COCl, and even more than NO_2.

Bromine Addition.—The reactions of methyl vinyl sulphone (I) and of *n*-butyl vinyl sulphone (II) have been studied in some detail, since they give a clear indication of the incursion of a new mechanism, which has not previously been demonstrable with certainty. The following table summarises the effect of catalysts (M/20) on the rate of reaction (k_2) between bromine (M/40) and the two sulphones:

	No catalyst.	H_2SO_4.	NaOAc.	LiCl.	HBr.	LiBr.	LiBr + NaOAc.
(I)	0·0011	—	—	0·023	0·045	0·091	—
(II)	0·0008	0·0015	0·0052 •	0·018	—	0·071	0·060

• Rising coefficients, due to elimination of the HBr from the reaction product.

These compounds react with bromine by a second-order mechanism (*e.g.*, for vinyl *n*-butyl sulphone: reactants M/40, k_2 = 0·0008; reactants M/20, k_2 = 0·0008). Lithium bromide is a

powerful catalyst for the reaction, and sodium acetate slightly reduces the rate of the lithium bromide-catalysed reaction. Both lithium chloride and hydrobromic acid also catalyse the reaction, but less powerfully than lithium bromide. Sodium acetate has some catalytic power, but sulphuric acid is relatively ineffective as a catalyst.

Olefinic compounds reacting by the electrophilic mechanism show with bromine in the concentration region M/40 a third-order reaction, which is considerably (usually some 300 times) slower than the corresponding reaction with chlorine. In the present case, a different type of reaction is clearly under observation, since the reaction is of the second order, and is some ten times faster than the corresponding chlorination. Previous results (*J.*, 1949, 297) were held to suggest that for olefinic compounds of the type $CH_2{:}CHX$, where X is a group with powerful electron-withdrawing characteristics, *e.g.*, CHO, NO_2, CN, bromine addition might proceed by a nucleophilic mechanism, in which the active reagent is the trihalide ion. The present results confirm these conclusions, and, in the authors' opinion, require the intervention in the catalysed reactions, of the ions Br_3^-, Br_2Cl^-, Br_2OAc^-, of diminishing stability, as shown by the diminishing effectiveness as catalysts of lithium bromide, lithium chloride, and sodium acetate.

It is to be emphasised that the reactions at present under consideration differ from those which in previous papers we have described as acid-catalysed additions, *e.g.*, to αβ-unsaturated acids, aldehydes, ketones, nitriles, and nitro-compounds. For these compounds, in contrast with the results given in the table above, sodium acetate reduces very considerably the rate of uncatalysed bromine addition, and sulphuric acid is an efficient catalyst. A proton-transfer to a basic group in the unsaturated compound is then a fundamental stage of such reactions, as illustrated by acid-catalysis of addition to crotonaldehyde [$k_3(H_2SO_4) = ca.$ 400; $k_3(NaOAc) = 0{\cdot}22$]. Similarly, Nozaki and Ogg (*J. Amer. Chem. Soc.*, 1942, **64**, 697, 704, 709) found for bromine addition to maleic and fumaric acids that hydrogen bromide was a much more efficient catalyst than lithium bromide.

The mechanism of the reaction described in this paper also seems to differ from those anion-catalysed reactions described by Swedlund and Robertson (*J.*, 1945, 141; 1947, 630) and by Nozaki and Ogg (*loc. cit.*) for addition to allyl chloride, vinyl bromide, and related substances. Bromine addition, under the conditions specified, appears, for the latter compounds, to be catalysed to a greater extent by lithium chloride than by lithium bromide, and this characteristic is maintained for compounds of widely different reactivity. The problem will be discussed in more detail in a following paper.

Our finding, that bromine addition to αβ-unsaturated sulphones is little catalysed by acids, suggests that the sulphone group (unlike the carbonyl, cyano-, and nitro-groups) is conjugated inefficiently with the double link, as also seems to be indicated for the ground state of the molecule (though not for excited states), both from theoretical considerations and from studies of the infra-red spectra of these compounds (Koch, *J.*, 1949, 409; Barnard, Fabian, and Koch, *ibid.*, p. 2442). The absence of conjugation between the sulphone group and the double link may also explain the fact that these compounds show little tendency to polymerise, whereas the related αβ-unsaturated aldehydes, acids, nitriles, and nitro-compounds, in which an electron-withdrawing group is certainly conjugated with the double link, readily polymerise. Nucleophilic addition of bromine to the αβ-unsaturated sulphones, therefore, appears to be caused solely by the strong inductive effect ($-I$) of the sulphonyl group, and this represents the simplest type of nucleophilic reaction which has been observed. The reaction with the bromine molecule alone is excessively slow, and in acetic acid solution may be due in part to the intervention of acetate ions. In general, all nucleophilic anions act as catalysts, according to the formulation:

$$X^- + Br{-}Br \rightleftharpoons [X{-}Br{-}Br]^- ; [X{-}Br{-}Br]^- + CH_2{:}CH{\cdot}SO_2Me \longrightarrow CH_2Br{\cdot}CHBr{\cdot}SO_2Me + X^-$$

Experimental.

The following compounds were used in this investigation: ethylenesulphonic acid, b. p. 120°/0·8 mm., n_D^{25} 1·405, n_D^{25} 1·451, neutralisation equiv., 110 (Calc.: 108); sodium ethylenesulphonate, from the acid and an equivalent amount of sodium acetate, in acetic acid solution; phenylethanesulphonyl chloride, m. p. 78·5°; sodium phenylethylenesulphonate, recrystallised before use (for these two compounds we are indebted to Professor F. G. Bordwell, North Western University, Illinois); methyl vinyl sulphone, b. p. 115—117°/19 mm.; n-butyl vinyl sulphone, b. p. 135°/15 mm. (for these two compounds we are indebted to Dr. G. D. Buckley, I.C.I., Northwich, Cheshire); the methyl compound was not further purified, but the butyl compound was redistilled before use, and the previously recorded b. p. was confirmed.

All measurements were made in duplicate or triplicate, specially ground and tested stoppered

bottles being used protected from light. Volatility corrections were applied to all chlorine reactions as previously described. Herewith are details of a typical rate determination:

M/40-CH_2:$CH{\cdot}SO_2Me$ + M/40-Br_2 + M/20-LiBr, in HOAc at 25°; 1-ml. samples titrated with M/80-$Na_2S_2O_3$.

Time (mins.)	0	50	160	230;	0	110	275	350
Titre (ml.)	4·02	3·58	2·93	2·63;	4·00	3·22	2·45	2·20

From the separate curves, $x = 20$, $t = 108$; $x = 20$, $t = 111$.

Additional results are expressed as times (minutes) for x% halogen absorption at 25° in acetic acid, unless otherwise stated:

M/40-CH_2:$CH{\cdot}SO_2Me$ + M/40-Br_2, $x = 10$, $t = 4050$; +M/10-H_2SO_4, $x = 10$, $t = 1580$; +M/20-LiCl, $x = 20$, $t = 435$; +M/5-LiBr, $x = 20$, $t = 123$; +M/10-LiBr, $x = 20$, $t = 110$; +M/20-LiBr, $x = 20$, $t = 110$; +M/40-LiBr, $x = 20$, $t = 129$; +M/80-LiBr, $x = 20$, $t = 173$; +M/160-LiBr, $x = 20$, $t = 276$; +M/20-LiBr + M/20-NaOAc, $x = 20$, $t = 130$; +M/20-HBr, $x = 20$, $t = 221$.

M/40-CH_2:$CH{\cdot}SO_2Bu$ + M/40-Br_2, $x = 10$, $t = 5710$; +M/20-H_2SO_4, $x = 20$, $t = 6220$; +M/20-NaOAc, $x = 20$, $t = 1920$; +M/20-LiCl, $x = 20$, $t = 555$; +M/20-LiBr, $x = 20$, $t = 141$. M/10-CH_2:$CH{\cdot}SO_2Bu$ + M/20-Cl_2, $x = 10$, $t = 11,600$; +M/20-NaOAc, $x = 10$, $t = 11,900$. M/20-CH_2:$CH{\cdot}SO_2Bu$ + M/20-Br_2, $x = 10$, $t = 2830$. From this last result and the value for reactants at M/40, $n = 2·0$.

M/10-CHPh:$CH{\cdot}SO_2Cl$ + M/20-Cl_2, $x = 20$, $t = 560$.

In addition to these neutral compounds, certain compounds ionised in acetic acid solution have also been examined:

M/80-CH_2:$CH{\cdot}SO_2H$ + M/80-Cl_2, $x = 20$, $t = 175$; M/10-CH_2:$CH{\cdot}SO_2H$ + M/80-Br_2, $x = 20$, $t = 1235$; +M/20-LiCl, $x = 20$, $t = 265$; M/80-CH_2:$CH{\cdot}SO_2Na$ + M/80-Cl_2 + M/80-NaOAc, $x = 20$, $t = 27·5$; M/80-CHPh:$CH{\cdot}SO_2Na$ + M/80-Cl_2, $x = 50$, $t = 0·80$; M/80-CHPh:$CH{\cdot}SO_2Na$ + M/80-Br_2, $x = 20$, $t = 12$; +M/20-LiCl, $x = 20$, $t = 8·75$.

The rates of bromine addition to CH_2:$CH{\cdot}SO_2H$ ($k_2 = 0·002$) and the more ionised CH_2:$CH{\cdot}SO_2Na$ ($k_2 = 0·006$), in comparison with the values for CH_2:$CH{\cdot}SO_2Me$, and the fact that the bromine rates are now slower than the chlorine rates, indicate that the nucleophilic reactions are in part obscured by electrophilic addition to the anions.

VICTORIA UNIVERSITY COLLEGE, WELLINGTON, NEW ZEALAND.

[*Received, June 8th*, 1950.]

---

550. *The Kinetics of Halogen Addition to Unsaturated Compounds. Part XXI. The Mechanisms of Addition Reactions.*

By P. B. D. DE LA MARE and P. W. ROBERTSON.

By altering the structure of the olefinic substance and the conditions of reaction, various mechanisms available for halogen addition have been identified, namely: (i) Electrophilic chlorine and bromine addition; (ii) electrophilic bromine addition catalysed by anions; (iii) nucleophilic bromine addition, catalysed by anions, and involving attack by ions of the type Br_3X^-; (iv) nucleophilic chlorine and bromine addition, catalysed by acids, and involving attack by halogen molecules, or more usually Br_3X^- ions, on cations of the type $^+$CHR·CH·A·BH, formed by co-ordination of a proton with a $(-I)$ group ·A:B which is conjugated with a double link. Reactions of type (iii) predominate over types (i) and (ii) only for rather unreactive olefins containing a powerfully deactivating $(-I)$ group; and those of type (iv) are important only in solvents which are poor proton acceptors (*e.g.*, acetic acid), are more readily observed for bromine than for chlorine addition, and depend to a considerable extent on the basicity of the group ·A:B, the groups CHO ≈ COPh > CN ≈ NO_2 > SO_2R being in order of decreasing effectiveness in promoting reaction by this mechanism.

OUR views concerning the detailed nature of halogen addition have, as the result of experimental development, gradually become modified since the first paper of this series (*J.*, 1937, 335). In particular, it has been discovered that the αβ-unsaturated sulphones may react with bromine by a particularly simple nucleophilic mechanism. It seems useful, therefore, to summarise, in conjunction with the preceding group of experimental papers, our present views concerning the various mechanisms available for these reactions of halogens, giving special emphasis to the nucleophilic processes (*i.e.*, those in which the halogenating agent is nucleophilic in character), which until recently have been imperfectly characterised. The results to which reference is made in the present paper have been determined in acetic acid as solvent, and are quoted as second-order rate coefficients (l. g.-mol.$^{-1}$ min.$^{-1}$), for $x = 20$% absorption of halogen, reactants M/80, at 25°, except where otherwise specified.

Electrophilic Addition.—(a) *Uncatalysed chlorine and bromine addition.* Chlorine addition, except in special circumstances, proceeds by a second-order process, and is subject to a small positive ionic-strength effect, electrolytes having a slight catalytic power for the reaction. The effect of structure on the rate of chlorine addition is consistent with the view that the reaction involves electrophilic attack by chlorine on the olefinic compound. Concerning the details of those stages of the mechanism which follow the initial attack by the chlorine molecule,* little is known, except that nucleophilic substances appear to be able to intervene in the addition process to give products other than the dichloro-compound. The intermediate involved in the reaction must, therefore, possess a carbonium centre, but it has not so far been ascertained with certainty whether a fully charged ionic intermediate is produced.

The comparative simplicity of chlorine addition has led us to use this process, wherever possible, as a standard of comparison for the study of constitutional effects. Bromine addition to all but the most unreactive olefins, in the concentration region M/40 at 25°, is of the first order with respect to the olefinic compound and of the second order with respect to bromine. Under the specified conditions, the rate ratio for chlorine to bromine addition is about 250, and is not very critically determined by the reactivity of the olefinic compound or by its structure. It is fairly certain, therefore, that the fundamental reaction involves again electrophilic attack by halogen, the function of the second molecule of bromine being, in all probability, that of assisting to break the Br–Br link in the attacking molecule (thus, in effect, forming Br_3^-), though whether this second molecule intervenes before or after the initial electrophilic attack is not determined. Intervention of nucleophilic substances to form mixed products also accompanies these third-order additions of bromine, and at still greater concentrations, reactions of a higher order with respect to halogen begin to take control, suggesting the participation of Br_4 molecules. In the reactions with bromine there is, as for chlorine, a small positive ionic-strength effect, as discussed in Part XIV (*J.*, 1949, 294).

It is noteworthy that the effects of substituents on these electrophilic processes show marked analogy with the effects of the same substituents on aromatic substitutions, and are in complete accord with the well-known classification of substituent groups given by Ingold. It is considered by Dewar ("Discussions of the Faraday Society," 1947, **2**, 51) that some olefinic substances are likely to react through "π-complex" intermediates (*e.g.*, the simplest ethylenes), whilst others form intermediates of another type (*e.g.*, butadiene, styrene, and related compounds). No such theoretical division of olefinic compounds into different categories has been revealed by our studies of the rates and mechanisms of halogen-addition reactions.

(b) *Anion-catalysed electrophilic bromine addition.* Another reaction process, the character of which has been reasonably well defined, involves, instead of participation of a second bromine molecule in the kinetics of the reaction, the intervention of an anion, giving such rate expressions as $-d[Br_2]/dt = k[A][Br_2][Cl^-]$, or $-d[Br_2]/dt = k[A][Br_2][Br^-] = k[A][Br_3^-]$. With excess of bromide ion, the reaction reaches a maximum rate, which is nearly identical for lithium bromide and for hydrogen bromide, when substantially all the bromine has been converted into Br_3^-. This mechanism is of greatest importance for compounds of the type $CHR{:}CH_2$, in which R is an atom or group having a $(+T, -I)$ effect.

In this type of reaction it is highly unlikely that Br_3^- or similar ions are the actual reactive halogenating species, as is shown by the effect of structure on the rate of reaction, in the following comparison :

Compound.	$CH_2{:}CH{\cdot}CH_2Cl$.	$CH_2{:}CH{\cdot}CH_2{\cdot}CN$.	$CH_2{:}CHBr$.
Rate (Br_2)	1·6	0·23	0·001
Rate (Br_2 + M/20-LiCl)	10	2·4	0·007

The total rate both of the catalysed and of the uncatalysed reaction decreases markedly as we proceed from allyl chloride to the many times less reactive vinyl bromide. If the $ClBr_3^-$ ion were the effective reagent in the catalysed reaction, then this ion would be required to react as a powerfully electrophilic reagent, judged by the effect of structure on reactivity. Such a hypothesis is rather unlikely. It is believed, therefore, that in the catalysed, as in the uncatalysed reaction, attack is initiated rather by the bromine molecule acting as an electrophilic reagent, the chloride ion rendering a subsequent stage in the addition process (which may actually be the completion of addition to form the chlorobromide of the olefinic compound) partially rate-determining.

If correction is made for the decreased concentration of free bromine in solutions containing also bromide ion, it is discovered that the catalytic power of different ions falls in the order

* Not, in these circumstances, the Cl^+ ion.

$Br^- > Cl^- > OAc^-$, the last being almost ineffective in catalysing addition by this mechanism. This is consistent with the experimentally observed order of the nucleophilic power of these ions in attacking some alkyl halides (cf. Bither, Sturtevant, and Thomas, *J. Amer. Chem. Soc.*, **1945**, **67**, 1562; Olson and Long, *ibid.*, 1936, **58**, 393; Young and Olson, *ibid.*, p. 1157; Beste and Hammett, *ibid.*, 1940, **62**, 2481).

Nucleophilic Addition.—(a) *Anion-catalysed nucleophilic addition.* For compounds in which the ethylenic link is deactivated, as far as attack by electrophilic reagents is concerned, by a substituent with a negative inductive effect (*e.g.*, for methyl vinyl sulphone), a different type of anion-catalysed addition has been observed. Addition of bromine to such compounds has been found to become more (instead of many times less) rapid than chlorine addition, and sodium acetate becomes a good catalyst for bromine addition, lithium chloride and, especially, lithium bromide being still better. The following table summarises these relationships:

Compound.	Cl_2.	Br_2.	Br_2 + NaOAc.	Br_2 + LiCl.	Br_2 + LiBr.
CH_2:CH·CH_2Cl	*ca.* 450	1·6	*ca.* 2	10	3·8
CH_2:$CHBr$	0·38	0·001	*ca.* 0·001	0·007	0·012
CH_2:CH·SO_2Me	0·0001	0·001	0·005	0·023	0·09

Vinyl bromide, as compared with methyl vinyl sulphone, for example, reacts some 10^3 times more rapidly when the reagent is chlorine, but less rapidly with bromine in the presence of lithium bromide. In the latter case, therefore, the reagent appears to be nucleophilic, and it is considered that the ions Br_2OAc^-, Br_2Cl^-, and Br_3^- are the active reagents in catalysed bromine addition to methyl vinyl sulphone. The existence of the first of these ions has not, as far as we are aware, been recognised, whereas Br_2Cl^- is known, and Br_3^- is still more stable (cf. Sidgwick, "The Chemical Elements and their Compounds," Oxford Univ. Press, 1950, Vol. II, p. 1193). It is consistent with the above that the order of catalytic power for reaction by this mechanism increases in the order NaOAc < LiCl < LiBr.

(b) *Acid-catalysed nucleophilic addition.* In the first paper of this series (*J.*, 1937, 335), it was shown that bromine addition to acrylic acid and to vinyl bromide is kinetically distinct from addition to other olefinic compounds such as allyl acetate, in that uncatalysed addition in acetic acid was autocatalytic, owing to the production of hydrogen bromide in the course of the reaction. Subsequent investigations by Anantakrishnan and his co-workers (*J.*, 1939, 224; *Chem. Reviews*, 1943, **33**, 27; *Proc. Indian Acad. Sci.*, 1946, **23**, *A*, 307, 312, 319; 1948, **27**, *A*, 184) extended our knowledge of the range of compounds for which this type of mechanism is available, without contributing significantly to our understanding of the nature of the catalysed reaction. Nozaki and Ogg (*J. Amer. Chem. Soc.*, 1942, **64**, 697, 704, 709) showed that the case of vinyl bromide must be considered separately from that of acrylic or maleic acid, the experimental distinction being that addition to vinyl bromide is catalysed equally by hydrogen and by lithium bromide. Addition to αβ-unsaturated acids, however, is very much more powerfully catalysed by hydrogen bromide than by lithium bromide. For these compounds, therefore, a proton appears to be required for the addition process. In the present series of papers, the importance of this mechanism of addition has been established for quinones, αβ-unsaturated ketones (*J.*, 1948, 980), acids (*J.*, 1945, 129), aldehydes (*J.*, 1945, 888), nitro-compounds (*J.*, 1947, 628), and nitriles (*J.*, 1950, 2834).

Numerous examples in which the order of reactivity with electrophilic reagents is reversed under conditions of acid catalysis (cf. *J.*, 1945, 129) show that these reactions involve attack by some nucleophilic halogenating agent. The specific influence of $(-T)$ groups conjugated with the double link in promoting acid-catalysis shows, however, that the nucleophilic halogenating agent is attacking, not the olefinic compound itself, but rather the ion produced by attachment of a proton to the substituent to form a mesomeric carbonium cation, as in the following formulation:

$$CH_2{:}CH{\cdot}CHO + \overset{+}{H} \rightleftharpoons CH_2{:}C\overset{+}{H}{\cdot}OH \longleftrightarrow \overset{+}{C}H_2{\cdot}CH{:}CH{\cdot}OH$$

This first stage of the reaction is favoured by electron-repelling substituents attached to the olefinic centre, *e.g.*, as in $CHPh_2{:}CH{\cdot}CHO$, whereas the subsequent nucleophilic attack by halogen on the resulting carbonium cation is hindered by such substituents. The balanced electronic requirements of the two stages make prediction in any particular instance difficult, but the experimental results now accumulated allow us to make certain generalisations concerning the relationship between constitution and the rate of acid-catalysed addition. In compounds of the type $CH_2{:}CHX$, the introduction of an alkyl or aryl group to form $CHR{:}CHX$ results in a decrease in rate, the stage of the reaction involving nucleophilic attack on the cation being predominant. On the other hand, in compounds of the type $CH_2{:}CHX$ and $CHR{:}CHX$,

when X is varied, it is found that the basicity of the group and its capacity for conjugation become important factors. Thus the groups COR > NO_2 > SO_2Me diminish in effectiveness as the basic character becomes less; the SO_2Me group is particularly ineffective, being, as discussed in Part XX (*J.*, 1950, 2836), inefficiently conjugated with the double linking.

Acid catalysis is absent, therefore for such compounds as allyl chloride, in which there is no basic group to attract a proton.* Acid catalysis may also be obscured when a powerfully electron-donating substituent is attached to the double link. In the case of cinnamic acid, for instance, the rate of electrophilic addition of bromine is sufficiently large to make catalysis of addition by added hydrobromic acid rather small, and difficult to distinguish from the alternatively available anion-catalysed reactions, whereas acrylic acid, owing to its low rate of electrophilic addition, shows very large acid catalysis.

The form in which the halogen takes part in acid-catalysed addition is shown by the catalytic power of different acids. Thus addition of bromine to cinnamaldehyde with different catalysts, M/320, arranged in order of decreasing conductivity in acetic acid, follows the following rate sequence (*J.*, 1945, 888):

Catalyst.	$HClO_4$.	HBr.	H_2SO_4.	HCl.	HNO_3.
Rate	7·3	*ca.* 300	3·4	24	*ca.* 0·5

The abnormal effectiveness of hydrogen chloride and especially of hydrogen bromide in relation to their acid strengths indicates that, although molecular bromine can, *e.g.*, in the presence of perchloric acid, act as a nucleophilic halogenating agent for a carbonium cation, yet the Br_3^- and the Br_2Cl^- ions are more powerful nucleophilic brominating agents, as indeed would be expected.

In earlier communications (*e.g.*, *J.*, 1945, 129), we considered the possibility that the active reagent in addition catalysed by hydrogen bromide might be the HBr_3 molecule, acting as a 1 : 4-brominating agent, and attacking simultaneously the unsaturated ($-T$) substituent and the double link. The establishment of similar catalysis of addition to αβ-unsaturated nitriles (*J.*, 1950, 2834), for which compounds steric considerations render unlikely such bimolecular addition of HBr_3 to an olefinic compound, suggests that this special mechanism is unnecessary. The following type of formulation, illustrated for an aldehyde, accords with the kinetics of the reaction for compounds with a $-I$, $-T$ group attached to the ethylene system:

$$CHR{:}CH{\cdot}CHO + H^+ \rightleftharpoons {}^+CHR{\cdot}CH{:}CH{\cdot}OH \overset{Br_3^-}{\rightleftharpoons} \underset{{}^+Br{-}Br}{CHR{\cdot}CH{:}CH{\cdot}OH} + Br^-$$

(I.) (II.)

$$(II) \longrightarrow \underset{{}^+Br{-}Br}{CHR{\cdot}\bar{C}H{\cdot}CH{\cdot}CH{:}O} \longleftrightarrow \underset{Br{-}Br}{\overset{+}{C}HR{\cdot}\bar{C}H{\cdot}CH{:}CH{:}O} \longrightarrow CHRBr{\cdot}CHBr{\cdot}CH{:}O$$

(III.) (IIIa.) (IV.)

Nucleophilic attack by Br_3^- on the organic cation (I) forms the intermediate (II), which then changes, by the removal of a proton, to form (III). An alternative resonance structure of (III) is (III*a*). What happens, in effect, is that the nucleophilic mechanism brings a bromine molecule into a position favourable sterically for the final electrophilic attack, and correspondingly there is *trans*-addition of bromine to the olefinic compound (cf. Nozaki and Ogg, *loc. cit.*), whereas *cis*-addition would be expected for a one-stage nucleophilic addition.

The proton required in the first stage of the reaction can be supplied either by the solvent or by any acid present in solution. Although the reaction is sensitive to small traces of hydrogen ions, being strongly decelerated by sodium acetate, large concentrations become unfavourable by maintaining a proton on the intermediate (II). The kinetics of the reaction thus correspond, for a given amount of acid catalyst, with the rate expression $-d[Br_2]/dt = k[A][Br_2]$, and the rate reaches a maximum value with added acids. Water added to the acetic acid solvent decreases the importance of this mechanism, by virtue of the greater stability of H_3O^+ than of H_2OAc^+, whereby protons become less readily available to form the reactive intermediate. Even for quite powerfully catalysed compounds, 25% of water in the solvent is sufficient almost completely to eliminate acid-catalysed bromination in favour of the electrophilic mechanism.

Chlorine addition can be forced to proceed by nucleophilic processes only in the most favourable circumstances. Certain αβ-unsaturated aldehydes, *e.g.*, cinnamaldehyde, with

* The ethylenic link itself is negligibly basic, even in acetic acid, despite the contrary view held by Anantakrishnan and his co-workers (*loc. cit.*).

chlorine and hydrochloric acid give evidence of acid catalysis. The rates of these catalysed additions, corrected for any concurrent electrophilic addition, are less than those of the corresponding acid-catalysed bromine additions, and this difference between the electrophilic and the nucleophilic process is an additional diagnostic of mechanism.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER ST., LONDON, W.C.1.
VICTORIA UNIVERSITY COLLEGE, WELLINGTON,
NEW ZEALAND.

[*Received, June 8th*, 1950.]

---

551. *Synthesis of Potential Antibacterial Agents. Part I. Some α-Alkylglutaric Acids and Their Derivatives.*

By JOHN C. ROBERTS and BERNARD SHAW.

A number of α-*n*-alkylglutaric acids and their anhydrides have been prepared. By treatment of the anhydrides with sulphanilamide and 2-aminothiazole, substituted glutaramic acids have been obtained. Some of these compounds have been tested for their tuberculostatic activity *in vitro*.

For reasons previously stated (Roberts, *Nature*, 1945, **155**, 697) it was thought that agaric acid—obtainable from the Basidiomycete, *Polyporus officinalis*, Vill.—might possess antibacterial activity towards *Mycobacterium tuberculosis*. Although the structure of agaric acid (α-*n*-hexadecylcitric acid) was established many years ago by degradative methods (Thoms and Vogelsang, *Annalen*, 1907, **357**, 145), no really satisfactory synthesis has yet been devised (cf., however, Passerini and Banti, *Chem. Zentr.*, 1931, I, 1432); so we decided to synthesise and investigate a number of compounds related in structure to agaric acid. This decision was strengthened by a consideration of the observations of Franke and Schillinger (*Biochem. Z.*, 1944, **316**, 313) who showed, during an investigation of a wide variety of organic compounds, that aliphatic acids can exert a marked influence on the metabolism of acid-fast bacteria, the nature of the influence depending *inter alia* on the length of the carbon chain. In this paper we describe the preparation and investigation of a number of α-*n*-alkylglutaric acids of varying chain-lengths and also of a number of derivatives containing, in addition to an acidic group, one of two potentially antibacterial groupings, 2-thiazolylcarbamyl or *p*-sulphamylphenylcarbamyl.

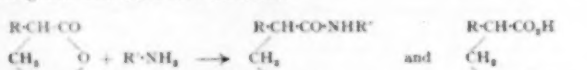
Very few α-alkylglutaric acids have been described. The α-methyl-, α-ethyl-, and α-propyl-acids have been prepared (Auwers and Titherley, *Annalen*, 1896, **292**, 209 *et seq.*; Mellor, *J.*, 1901, **79**, 128) by simultaneous hydrolysis and decarboxylation of the appropriate triethyl alkane-1 : 1 : 3-tricarboxylate by heating it under reflux with strong mineral acid. We found this method to be inapplicable to higher members of the series. α-*n*-Octylglutaric acid has been made by Kögl, Erxleben, *et al.* (*Z. physiol. Chem.*, 1935, **235**, 198) using the acetoacetic ester route, which, however, suffers from the disadvantage that ketones are concomitantly produced. We found the following method to be the most advantageous and to be applicable to the synthesis of an α-alkylglutaric acid of any chain-length. The required alkane-1 : 1 : 3-tricarboxylate—readily prepared from an alkylmalonic ester and β-iodopropionic ester—was hydroysed with an alcoholic solution of potassium hydroxide, and the tricarboxylic acid isolated and then decarboxylated at 180—190°. The product was then heated with aqueous alkali (to hydrolyse some anhydride which was always formed) before the dicarboxylic acid was isolated.

The cyclic anhydrides could not be prepared by heating the α-alkylglutaric acids. Although some water was eliminated by this treatment, analysis showed that the products were not the desired anhydrides but presumably linear anhydrides of possible type

$$R{\cdot}CH(CO_2H){\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CHR{\cdot}CO{\cdot}O{-}$$

etc. However, the cyclic anhydrides were readily obtained by treatment of the alkylglutaric acids with excess of acetic anhydride.

By treatment of these anhydrides in an organic solvent with primary amines, mixtures of *N*-substituted glutaramic acids were obtained :



(R = *n*-alkyl; R′ = 2-thiazolyl- or *p*-sulphamylphenyl-.)

Separation of the isomers by fractional crystallisation proved very difficult and in some cases only one isomer was isolatable. Unfortunately, it is not possible to allocate unambiguous structures to the compounds obtained. In the case of phenylsuccinic anhydride Anschütz *et al.* (*Annalen*, 1907, **354**, 117) were able to derive a generalisation whereby the structure of the derivatives could be predicted with some certainty, for the amino- or substituted-amino-residue attached itself to the carbonyl group corresponding to the " weaker " carboxyl group in the parent dicarboxylic acid, *i.e.*, to the carboxyl group further removed from the phenyl substituent. We considered this generalisation to be inapplicable to our compounds, first because it was not possible to determine which of the two acid groupings was the weaker, and secondly because in most cases two isomers were concomitantly produced. This problem has remained unsolved.

None of the compounds tested showed notable tuberculostatic activity. We wish to thank Dr. W. C. Tobie (private communication) for informing us that agaric acid, even in a concentration of 1 in 1560, failed to inhibit the growth *in vitro* of a human virulent strain of *M. tuberculosis*. We are greatly indebted to Messrs. Boots Pure Drug Co. for determining the tuberculostatic activities (see below) of some of the synthetic compounds. It is noteworthy that, in the one instance where the two isomers of an *N*-substituted glutaramic acid were tested, no difference in tuberculostatic activity was observed.

Experimental.

[The figures given for tuberculostatic activity represent dilutions, in thousands, at which complete inhibition of the growth of *M. tuberculosis* (human virulent strain) was maintained for 4 weeks in modified Long's medium, the floating pellicle method being used. Figures in parentheses represent dilutions at which partial inhibition occurred. All the tests were carried out in presence of serum.]

Starting Materials.—All the required ω-alkylmalonic esters were prepared by the usual procedure from ethyl malonate and the appropriate ω-alkyl halides. The latter, except tetradecyl iodide, were obtained commercially (or prepared from the appropriate alcohols) and, after drying, were fractionally distilled to give compounds with a maximum distillation range of 3°.

n-*Tetradecyl Iodide.*—Ethyl myristate (prepared from " technical " myristic acid) was distilled *in vacuo*, an electrically heated fractionating column being used, and the fraction of b. p. 164—166°/10 mm. was collected (Phillips and Mumford, *J.*, 1932, 902, give b. p. 139°/4 mm.). ω-Tetradecyl alcohol, obtained by reduction of the ester (Bouveault–Blanc method), was converted into ω-tetradecyl iodide by treatment with red phosphorus and iodine.

Ethyl β-Iodopropionate.—Ethyl β-chloropropionate, prepared from ethyl acrylate and dry hydrogen chloride (Moureu, Murat, and Tampier, *Ann. Chim.*, 1921, **15**, 239), was converted into ethyl β-iodopropionate by treatment with dry sodium iodide in dry acetone (King and L'Ecuyer, *J.*, 1934, 1903).

General Procedure for the Preparation of 1 : 3 : 3-*Tricarbethoxyalkanes.*—Finely divided sodium (1 atom) was covered with a sufficient quantity of dry ether to act as medium for the reaction. The ethyl ω-alkylmalonate (1 mol.), dissolved in a little dry ether, was gradually added and the mixture heated under reflux until all the sodium had disappeared. After the mixture had been cooled, ethyl β-iodopropionate (1·02 mols.) was slowly added. A vigorous reaction ensued and sodium iodide separated. The reaction was completed by boiling under reflux until the reaction mixture became neutral to moist litmus-paper. To the cooled mixture, water was added (to dissolve the sodium iodide), and the ethereal layer separated. The aqueous layer was extracted with ether. The ethereal solutions were combined, washed once with water, dried (Na_2SO_4), and the ether evaporated. The residue was distilled *in vacuo* and, after removal of any remaining starting material, the required 1 : 3 : 3-*tricarbethoxyalkane* was collected as a high-boiling fraction. The compounds so obtained (see table) were colourless, viscous oils (or solids of low m. p.) with a faintly rancid odour.

1 : 3 : 3-*Tricarbethoxyalkanes*, $CH_3{\cdot}[CH_2]_n{\cdot}C(CO_2Et)_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Et$.

				Found, %		Reqd., %	
n.	Yield, %.	B. p./mm.	Formula.	C.	H.	C.	H.
1	50	170—174°/12 [a]	—	—	—	—	—
2	39	160—166/7 [b]	—	—	—	—	—
3	64	176—180/9	$C_{14}H_{24}O_6$	60·2	9·1	60·7	8·9
4	62	148—153/2	$C_{17}H_{30}O_6$	61·5	9·0	61·8	9·2
5	67	164—167/2	$C_{18}H_{32}O_6$	62·7	9·1	62·8	9·4
6	67	166—169/1·5	$C_{19}H_{34}O_6$	63·7	9·3	63·7	9·6
7	67	180—184/1·5	$C_{20}H_{36}O_6$	64·5	9·7	64·5	9·7
9	49	193—198/1	$C_{22}H_{40}O_6$	65·6	10·2	66·0	10·1
11	50	210—215/1·5	$C_{24}H_{44}O_6$	66·9	9·9	67·3	10·4
13	78	226—230/2 (m. p. 30°)	$C_{26}H_{48}O_6$	68·5	10·6	68·4	10·6
15	54	249—253/1·8 (m. p. 35·5°)	$C_{28}H_{52}O_6$	69·1	11·0	69·4	10·8

[a] Auwers and Titherley, *Annalen*, 1896, **292**, 213, give b. p. 180°/25 mm.
[b] Mellor, *J.*, 1901, **79**, 129, gives b. p. 180—185°/32 mm.

ω-n-*Alkylglutaric Acids.*—The ω-ethyl- and ω-*n*-propyl-glutaric acids were prepared from the corresponding tricarbethoxyalkanes by heating the latter under reflux with concentrated hydrochloric

acid. The remaining acids were prepared by the following technique. The tricarbethoxyalkane (1 mol.) and a 25% solution of potassium hydroxide (3·3 mols.) in ethanol (95%) were boiled under reflux for 3—5 hours. The alcohol was distilled off, the residue dissolved in water, and the solution acidified. The oil which separated was collected by four extractions with ether. The combined extracts were washed with water, dried ($MgSO_4$), and filtered. Evaporation of the ether yielded the tricarboxylic acid (as a light brown gum), which was decarboxylated by heating it at 190° until evolution of carbon dioxide ceased. The crude dicarboxylic acid (1 mol.)—containing some anhydride as impurity—was boiled under reflux with a 20% aqueous solution of potassium hydroxide (*ca.* 2·5 mols.) until a clear solution was obtained (3—4 hours). The solution was cooled, strongly acidified with concentrated hydrochloric acid, and extracted three times with ether. The combined ethereal extracts were washed once with water, and dried ($MgSO_4$), and the ether evaporated *in vacuo*. The residual gums crystallised after treatment by usual methods and the α-*n*-alkylglutaric acids were recrystallised to constant m. p.s from suitable solvents. The *acids* (see table) so obtained are colourless, crystalline solids of low m. p. and of sparing solubility in water. The solubility in water decreases with increasing chain-length (100 g. of water at 20° dissolve 81 mg. of α-*n*-hexadecylglutaric acid).

α-n-*Alkylglutaric acids*, $CO_2H{\cdot}CH_2{\cdot}CH_2{\cdot}CHR{\cdot}CO_2H$.

	Solvent for				Found.			Required.			Tuberculostatic
R.	recrystn.[a]	M. p.	Yield, %.[a]	Formula.	C, %.	H, %.	Equiv.[b]	C, %.	H, %.	Equiv.	activity.
Et[c]	A	60·5°	66	—	—	—	—	—	—	—	—
Pr[d]	A	70	72	—	—	—	—	—	—	—	—
Bu	B	41	46	$C_9H_{16}O_4$	57·8	8·3	94·0	57·4	8·6	94·1	0
Am[e]	—	27—28	44	$C_{10}H_{18}O_4$	59·5	9·3	101·8	59·4	9·0	101·1	—
C_8H_{19}	B	37·5	40	$C_{13}H_{24}O_4$	61·4	9·4	109·4	61·1	9·3	108·1	—
C_7H_{15}	C	47	53	$C_{12}H_{22}O_4$	62·3	9·5	116·3	62·6	9·6	115·2	0
C_8H_{17}[f]	C	50·5	45	$C_{13}H_{24}O_4$	63·3	9·8	121·6	63·9	9·9	122·2	0 (1)
$C_{10}H_{21}$	C	57·5	45	$C_{15}H_{28}O_4$	66·0	10·4	—	66·2	10·4	—	—
$C_{15}H_{31}$	B	71·5	44	$C_{17}H_{32}O_4$	67·9	10·7	149·2	68·0	10·7	150·2	—
$C_{14}H_{29}$	D	77·5	63	$C_{16}H_{30}O_4$	69·2	10·9	—	69·5	11·1	—	—
$C_{16}H_{33}$	D	78	45	$C_{21}H_{40}O_4$	70·3	10·9	177·2	70·7	11·3	178·3	—

[a] Calc. on the tricarbethoxyalkane. [b] By the silver salt method. [c] Auwers and Titherley, *loc. cit.*, give m. p. 60·5°. [d] Mellor, *loc. cit.*, gives m. p. 66—68°. [e] Crystallisation was achieved by cooling in alcohol–solid carbon dioxide. [f] Kögl, Erxleben, *et al.*, *loc. cit.*, give m. p. 48°.
[a] A = Water; B = benzene; C = light petroleum (b. p. 40—60°); D = light petroleum (b. p. 60—80°).

α-n-*Alkylglutaric Anhydrides*.—All attempts to prepare cyclic anhydrides by distillation *in vacuo* of α-*n*-hexyl-, -decyl-, -dodecyl-, -tetradecyl-, or -hexadecyl-glutaric acid were unsuccessful. For example, when α-*n*-tetradecylglutaric acid (4·5 g.) was distilled *in vacuo*, a fraction (3·5 g. of colourless oil) of b. p. 259—262°/15 mm. was obtained which, when cooled, deposited colourless crystals of m. p. 46·5° (Found: C, 71·2; H, 11·1. Calc. for $C_{19}H_{34}O_3$: C, 73·5; H, 11·0. Calc. for the parent acid, $C_{19}H_{36}O_4$: C, 69·5; H, 11·1%). Repeated distillation gave similar results. Fractional crystallisation of the product from light petroleum (b. p. 40—60°) yielded no pure compound.

The following procedure gave pure cyclic anhydrides in good yield. The α-*n*-alkylglutaric acid was heated under reflux for 45 minutes with approximately five times its weight of acetic anhydride. The acetic acid and excess of acetic anhydride were removed at 65° *in vacuo*. In the preparation of α-*n*-butyl- and α-*n*-hexyl-glutaric anhydrides the residues were distilled *in vacuo*; in other cases (see table) the residues, when chilled, deposited crystals of the anhydrides which were recrystallised from light petroleum (b. p. 40—60°). The α-*n*-*alkylglutaric anhydrides* are colourless viscous oils or colourless solids which separate from light petroleum as pearly lustrous plates.

α-n-*Alkylglutaric anhydrides*, $CH_2\langle{}^{CHR\cdot CO}_{CH_2\cdot CO}\rangle O$.

				Found, %.		Req., %.	
R.	M. p. (or b. p.).	Yield, %.	Formula.	C.	H.	C.	H.
C_4H_9	(170—172°/12 mm.)	76	$C_9H_{14}O_3$	62·5	8·1	62·1	8·3
C_5H_{10}	(195—197°/14 mm.)	80	$C_{10}H_{16}O_3$	66·1	9·1	66·7	9·1
C_7H_{15}	36°	67	$C_{12}H_{20}O_3$	67·8	9·3	67·9	9·5
C_8H_{17}	42·5°	49	$C_{13}H_{22}O_3$	69·0	9·6	69·0	9·8
$C_{10}H_{21}$	51°	57	$C_{15}H_{26}O_3$	70·5	10·0	70·8	10·3
$C_{12}H_{25}$	58·5°	70	$C_{17}H_{30}O_3$	71·8	10·7	72·3	10·7
$C_{14}H_{29}$	62·5°	90	$C_{19}H_{34}O_3$	73·7	10·9	73·5	11·0
$C_{16}H_{33}$	69°	85	$C_{21}H_{38}O_3$	74·2	11·1	74·5	11·3

3(*or* 1)-(p-*Sulphamylphenylcarbamyl*)-n-*alkane*-1(*or* 3)-*carboxylic Acids*.—The *n*-alkylglutaric anhydride (1 mol.) and sulphanilamide (1·05 mols.) were dissolved in about twenty times their combined weight of dry acetone and the solvent was expelled by warming on the steam-bath. The residual syrup, when cooled, yielded a light brown solid which was washed with water, with 2*N*-hydrochloric acid, and finally with water again until the washings were free from chloride ion. The crude *acids* were dried and recrystallised from acetone (see table). By a similar procedure, attempts were made to prepare higher members of this series. Crystalline products were obtained which had correct analyses but melted over a range of about 40°. These products were intractable mixtures of the two possible isomers.

3(*or* 1)-(p-*Sulphamylphenylcarbamyl*)-n-*alkane*-1(*or* 3)-*carboxylic acids*, $NH_2{\cdot}SO_2{\cdot}C_6H_4{\cdot}NH{\cdot}CO{\cdot}CHR{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$ *or* $NH_2{\cdot}SO_2{\cdot}C_6H_4{\cdot}NH{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CHR{\cdot}CO_2H$.

R.	M. p.	Yield, %.	Formula.	Found, %. N.	Found, %. S.	Reqd., %. N.	Reqd., %. S.	Tuberculostatic activity.
C_9H_{19}	176—178°	30	$C_{19}H_{30}O_5N_2S$	7·1	—	7·0	—	0 (5)
$C_{11}H_{23}$	169—175	68	$C_{21}H_{34}O_5N_2S$	6·8	7·7	6·6	7·5	—
$C_{13}H_{27}$	171—174	64	$C_{23}H_{38}O_5N_2S$	6·3	7·3	6·2	7·1	1 or 0 (5)

3(*or* 1)-(2-*Thiazolylcarbamyl*)-n-*alkane*-1(*or* 3)-*carboxylic Acids*.—Equimolecular quantities of the alkylglutaric anhydride and of 2-aminothiazole were dissolved in dry, alcohol-free chloroform, and the solvent was expelled by warming the solution on the steam-bath. An ethereal solution of the cooled, oily residue was twice extracted with 2*N*-sodium hydroxide, and the ethereal layer was discarded. To the combined alkali extracts was added excess of 2*N*-hydrochloric acid. The *N*-substituted amic acid was collected in ether (3 extractions); the ethereal solution was washed with water and dried ($MgSO_4$). Evaporation of the ether *in vacuo* yielded a crystalline solid which was recrystallised to constant m. p. In the cases of the derivatives of *n*-heptadecane and *n*-nonadecane the residues obtained by evaporation of the chloroform yielded, on cooling, a light brown gum and a light brown solid, respectively. These residues proved to be mixtures of isomers from which, in both cases, the isomers of lower m. p. were extracted with ether. Data relating to the *acids* are in the following table.

3(*or* 1)-(2-*Thiazolylcarbamyl*)-n-*alkane*-1(*or* 3)-*carboxylic acids*, $(C_3H_3NS)NH{\cdot}CO{\cdot}CHR{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$ or $(C_3H_3NS)NH{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CHR{\cdot}CO_2H$.

R.	Solvent for recrystn.	M. p.	Yield, %.	Formula.	Found, %. N.	Found, %. S.	Reqd., %. N.	Reqd., %. S.	Tuberculostatic activity.
C_9H_{19}	EtOH [a]	156—157°	14	$C_{15}H_{23}O_3N_3S$	10·4	—	10·4	—	0 (1)
C_9H_{19}	(i) EtOH; (ii) aq. EtOH	154—156	10	$C_{15}H_{23}O_3N_3S$	9·6	—	9·4	—	—
$C_{11}H_{23}$	EtOH	158—161	19	$C_{17}H_{27}O_3N_3S$	9·1	—	9·0	—	1 (5)
$C_{11}H_{23}$ [b]	EtOH	108—111	4·6	$C_{17}H_{27}O_3N_3S$	9·0	—	9·0	—	—
$C_{13}H_{27}$	COMeEt	157—159	13·5	$C_{19}H_{31}O_3N_3S$	6·6	7·7	6·8	7·8	1 (5)
$C_{13}H_{27}$	aq. EtOH	98—100	13·5	$C_{19}H_{31}O_3N_3S$	7·0	—	6·8	—	1 (5)
$C_{15}H_{31}$	$CHCl_3$	154—157	19	$C_{21}H_{35}O_3N_3S$	6·4	—	6·4	—	—
$C_{15}H_{31}$	EtOH	88—89	7·7	$C_{21}H_{35}O_3N_3S$	6·1	—	6·4	—	—

[a] In this table "EtOH" means white industrial methylated spirit.
[b] Isomer obtained as a second fraction in the second recrystallisation.

We thank Miss S. Hastings, B.Sc., for performing a large number of microanalyses.

THE UNIVERSITY, NOTTINGHAM. [*Received, June 16th*, 1950.]

---

552. *Chemistry of the Vitamin B_{12} Group. Part I. Acid Hydrolysis Studies. Isolation of a Phosphorus-containing Degradation Product.*

By J. G. BUCHANAN, A. W. JOHNSON, J. A. MILLS, and A. R. TODD.

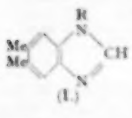
The acid hydrolysis of vitamin B_{12} has been examined in detail. The experimental conditions for the formation of 5 : 6-dimethylbenziminazole and two *N*-substituted 5 : 6-dimethylbenziminazoles have been ascertained, as well as for the preparation of the basic hydrolysis product giving a positive ninhydrin reaction. Similar degradations have been carried out with another member of the vitamin B_{12} group, vitamin B_{12c}, which differs from vitamin B_{12} only in the portion of the molecule represented by the red cobalt-containing hydrolysis product. The location of the phosphorus atom in vitamins B_{12} and B_{12c} has been determined by the isolation, in the form of its barium salt, of a *N*-substituted 5 : 6-dimethylbenziminazole bearing a phosphorylated side-chain. Removal of the phosphoryl group yields a glycoside, evidently identical with 5 : 6-dimethyl-1-α-D-ribofuranosylbenziminazole (Brink, Holly, Shunk, Peel, Cahill, and Folkers, *J. Amer. Chem. Soc.*, 1950, **72**, 1866). The two *N*-substituted benziminazoles obtained on hydrolysis of the vitamin are thus inter-related in a manner exactly analogous to the pyrimidine and purine nucleotides and nucleosides. A new method of synthesis of benziminazole *N*-glycosides is described.

A CRYSTALLINE anti-pernicious anæmia factor was isolated from liver independently by Rickes, Brink, Koniuszy, Wood, and Folkers (*Science*, 1948, **107**, 396; **108**, 134) and by Lester Smith and his colleagues (*Nature*, 1948, **161**, 638; **162**, 144; *Proc. Roy. Soc.*, 1949, *B*, **136**, 502). Later isolations from the same source were reported by Ellis, Petrow, and Snook (*J. Pharm. Pharmacol.*, 1949, **1**, 60) and by Pierce, Page, Stokstad, and Jukes (*J. Amer. Chem. Soc.*, 1949, **71**, 2952). Lester Smith *et al.* used as a bioassay in their isolation procedure the clinical effect on patients suffering from pernicious anæmia. Rickes *et al.*, on the other hand, employed a microbiological

assay based on the effect of the factor on the growth of certain organisms, notably *Lactobacillus lactis* Dorner; no doubt for this reason they described the isolated anti-pernicious anæmia factor as vitamin B_{12}, a name which has been generally adopted. The discovery that vitamin B_{12} could also be isolated from the culture fluid of *Streptomyces griseus* (Rickes *et al.*, *Science*, **1948**, **108**, 634) has led to a somewhat greater availability of the vitamin, which is now being increasingly used in clinical practice. Vitamin B_{12} is closely related to the previously described animal protein factor of Jukes *et al.* (*J. Biol. Chem.*, **1949**, **180**, 647, and earlier papers).

Since the latter part of **1948** we have carried out a series of investigations on the material isolated from liver and kindly supplied by Dr. Lester Smith of Glaxo Laboratories Ltd., and by Dr. T. H. Jukes of Lederle Laboratories Inc. The very small amounts of material available, particularly in the early stages, considerably hampered chemical investigation and we devoted most of our attention to the acid hydrolysis of the vitamin, a reaction which has been the subject of most of the work published so far by other investigators. Vitamin B_{12}, which forms dark red needles, owing their colour, in part at least, to the molecule containing co-ordinately bound cobalt, was ascribed a formula $C_{61-64}H_{88-89}O_{13}N_{14}PCo$ by Brink, Wolf, Kaczka, Rickes, Koniuszy, Wood, and Folkers (*J. Amer. Chem. Soc.*, **1949**, **71**, 1854). Our material, dried to constant weight *in vacuo* at room temperature, gave analytical values corresponding approximately to a formula $C_{63}H_{91}O_{20}N_{14}PCo$, which has a higher content of hydrogen and oxygen than that of the American workers, but since their sample was dried at 100° the difference is probably caused merely by a greater degree of hydration in our analytical sample. The identity of the two preparations of the vitamin dried under the same conditions has been established by direct comparison (Fantes, Page, Parker, and Lester Smith, *Proc. Roy. Soc.*, *loc. cit.*). In early experiments on the acid hydrolysis of slightly impure specimens of vitamin B_{12}, we observed the presence of various common amino-acids in the hydrolysate but quickly found that these acids derived from the impurities and were not formed when the pure vitamin was hydrolysed. When pure vitamin B_{12} was heated with 6*N*-hydrochloric acid at 100° for 48 hours there were produced (1) phosphoric acid, (2) ammonium chloride, (3) a colourless compound showing no selective absorption in the ultra-violet region but giving a purple colour with ninhydrin, (4) two colourless compounds with characteristic ultra-violet absorption spectra but giving no reaction with ninhydrin, and (5) a deep-red non-crystalline material containing co-ordinately bound cobalt. These results agree in the main with those of other workers. The substance (2) giving the ninhydrin reaction has been obtained also by Ellis, Petrow, and Snook (*loc. cit.*); although it was at first thought by them (*ibid.*, **1949**, **1**, 735, 950) to be 2-amino-1-propanol on the basis of its behaviour on paper chromatograms, they later withdrew their claim (*ibid.*, **1950**, **2**, 128) when they failed to obtain alanine from it on permanganate oxidation. Using the technique of paper chromatography and applying the method of Crumpler and Dent (*Nature*, **1949**, **164**, 441) involving the formation of copper complexes, we have shown that the base (2) is not an α-amino-acid and, since treatment of it with nitrous acid and then 4*N*-hydrochloric acid yields a product which no longer reacts with ninhydrin, we conclude that it contains a primary rather than a secondary amino-group. The similarity between the behaviour of substance (2) and certain alkanolamines has also been confirmed by us, but identification by paper chromatography alone seems dangerous, especially when compounds such as 2-amino-1-propanol and 1-amino-2-propanol have virtually the same R_F value in various solvents. We are in full agreement with Ellis, Petrow, and Snook that the base (2) is an authentic degradation product of vitamin B_{12} and that it is produced in substantial quantity under the conditions of hydrolysis from which Brink *et al.* (*loc. cit.*) apparently failed to detect it.*

Brink and Folkers (*J. Amer. Chem. Soc.*, **1949**, **71**, 2951) isolated from acid hydrolysates of vitamin B_{12} a crystalline degradation product which they identified as 5:6-dimethylbenziminazole (I; R = H); on this basis vitamin B_{12} was ascribed a structure (I; R = $C_{53-54}H_{77-81}O_{13}N_{12}PCo$).



(I.)

Holiday, Petrow, *et al.* (*J. Pharm. Pharmacol.*, **1949**, **1**, 734, 957) identified the same compound (I; R = H) in acid hydrolysates by its characteristic absorption spectrum. They obtained evidence for the presence in their hydrolysates of two further unidentified materials which seemed on spectroscopic evidence to be *N*-substituted 5:6-dimethylbenziminazoles. These two unidentified

* Since this paper was written, the base has been identified as D-1-amino-2-propanol (Wolf, Jones, Valiant, and Folkers, *J. Amer. Chem. Soc.*, 1950, **72**, 2820). Furthermore, Chargaff, Levine, Green, and Kream (*Experientia*, 1950, **6**, 229) have shown that the ratio, aminopropanol produced on hydrolysis : phosphorus in vitamin B_{12} is two to one.

substances we believe to be identical with the two compounds which we obtained as fraction (4) in our hydrolysis experiments described above. Under the conditions of hydrolysis specified by Holiday and Petrow (*loc. cit.*) or in the experiments mentioned above, we have never obtained any of the simple benziminazole derivative (I; R = H); we have, however, obtained it by hydrolysis under more vigorous conditions (16 hours at 150° with 6N-hydrochloric acid).

The supplies of vitamin B_{12} isolated from liver and available to us were too limited to permit of adequate degradative studies involving isolation of the colourless hydrolysis products as distinct from their study by such techniques as paper chromatography, but the recognition that there exist several closely related " vitamins B_{12} " has recently made possible an extension of our investigations and we have devoted our main attention to a new member of the vitamin B_{12} group, for which the name vitamin B_{12a} is proposed. The existence of more than one red clinically active factor in liver extracts was first recognised by Lester Smith and his colleagues (*loc. cit.*), and the crystallisation of a second active compound from this source has been reported from the Lederle Laboratories (Pierce, Page, Stokstad, and Jukes, *loc. cit.*). Biologically, this new compound was indistinguishable from the original vitamin B_{12} in its effect on the growth of *L. leichmanii* 313 (Hoffmann, Stokstad, Hutchings, Dornbush, and Jukes, *J. Biol. Chem.*, 1949, **181**, 635) and in the chick assay (Stokstad, Jukes, Pierce, Page, and Franklin, *ibid.*, 1949, **180**, 647), and it was named by its discoverers vitamin B_{12b}. A similar product was also obtained from cultures of *S. aureofaciens* used for the production of aureomycin (Stokstad *et al.*, *loc. cit.*; *Fed. Proc.*, 1950, **9**, 235) and from *S. griseus* cultures (Fricke, Lanius, de Rose, Lapidus, and Frost, *ibid.*, p. 173). The name vitamin B_{12b} was selected because B_{12a} had been earlier applied to a product which had been obtained by Kaczka, Wolf, and Folkers (*J. Amer. Chem. Soc.*, 1949, **71**, 1514) by catalytic hydrogenation of vitamin B_{12} followed by aerial oxidation and was reported to have only some 20% of the activity of the original vitamin when assayed using *L. leichmanii* 313. Whether vitamin B_{12a} does in fact represent merely an impure preparation of vitamin B_{12b}, as has been claimed by Pierce, Stokstad, Jukes, *et al.* (*J. Amer. Chem. Soc.*, 1950, **72**, 1042, 2615), has not yet been finally established.

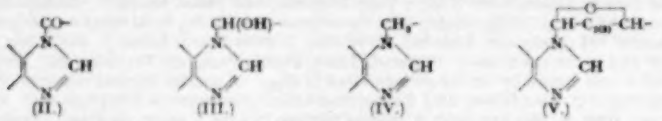
Vitamin B_{12c} is quite distinct from any of the factors so far discussed. It has been supplied to us by Dr. Lester Smith of Glaxo Laboratories Ltd., who has produced it from culture broths of *S. griseus*. Full details of its isolation and its relationship to other members of the B_{12} group will be published elsewhere, but its activity in promoting the growth of *L. lactis* Dorner ATCC 8000 (Cuthbertson *et al.*, *Biochem. J.*, 1949, **44**, v) and *L. leichmanii* 313 (Lees and Emery, *ibid.*, **45**, ii) is similar to that of vitamin B_{12} and it is also highly active clinically in the treatment of pernicious anæmia. Vitamin B_{12c} is the " unnamed factor " mentioned in papers by Lester Smith and Ungley, and by Mollin and Dacie at a meeting of the Royal Society of Medicine on February 14th, 1950 (*Lancet*, 1950, **i**, 353; *Proc. Roy. Soc. Med.*, in the press) and at times referred to as vitamin B_{12a}. Crystallised in the same way as vitamin B_{12} itself, vitamin B_{12c} forms dark red needles and gives analytical values approximating to a formula $C_{63}H_{91}O_{22}N_{14}PCo$, *i.e.*, it appears to be more highly oxygenated than vitamin B_{12} which it otherwise closely resembles.

We are at present engaged on a detailed investigation into the structure of vitamin B_{12c}, and some of our results concerning its behaviour on acid hydrolysis are now presented. It should be emphasised that, although our results refer strictly to vitamin B_{12c}, careful comparisons with vitamin B_{12}, treated under identical conditions, have revealed no differences in behaviour in so far as the colourless products of hydrolysis are concerned; the difference between the two vitamins seems to concern that part of the molecule which is represented by the red cobalt-containing fission product. Acid hydrolysis of vitamin B_{12c} yields, in addition to phosphoric acid, ammonia, the base giving a positive ninhydrin reaction, and a red amorphous product, three substances all of which appear to be benziminazole derivatives (cf. Holiday and Petrow, *loc. cit.*). Of these three, one is 5 : 6-dimethylbenziminazole and is produced only under drastic conditions of hydrolysis (150° for 5—16 hours with 6N-hydrochloric acid), while the other two are the more complex substances which, on the evidence of Holiday and Petrow (*loc. cit.*), have been regarded as *N*-substituted 5 : 6-dimethylbenziminazoles; we will refer to the more and the less complex of these compounds as the α- and β-benziminazole respectively, as has been done by Holiday and Petrow.

The α-benziminazole is the sole colourless product showing strong ultra-violet absorption when vitamin B_{12c} is hydrolysed under relatively mild conditions, *e.g.*, with N-hydrochloric acid at 100° for 1—20 hours. We have isolated this substance in the form of its barium salt and shown it to be a substituted phosphoric acid. Further hydrolysis of the α-benziminazole, or hydrolysis of the original vitamin B_{12c} under more vigorous conditions (100° for 48 hours with

6N-hydrochloric acid), gives the phosphorus-free β-benziminazole accompanied by some of the unchanged α-compound, and still more drastic hydrolysis yields the unsubstituted 5 : 6-dimethylbenziminazole. These reactions suggest that the α-benziminazole contains a phosphorylated side-chain attached to one of the nitrogen atoms in the benziminazole nucleus and that the β-benziminazole contains the same side-chain without the phosphoryl group; this is in accordance with the behaviour of the compounds on paper chromatography and with their absorption spectra. Our efforts have therefore been directed towards determining the nature and mode of attachment of this side chain and the position of the phosphoryl group.

Analysis of the barium salt of the α-benziminazole indicates a formula $C_{14}H_{17}O_7N_2PBa,H_2O$ or $C_{14}H_{19}O_8N_2PBa,H_2O$ from which it may be surmised that the side-chain grouping of five or six carbon atoms bears several hydroxy-groups as well as a phosphoryl residue. If this side-chain is assumed to be attached to nitrogen, the simplest types of linkage which might be involved are represented by the partial structures (II), (III), (IV), and (V). Of these, (II) and



(II.) (III.) (IV.) (V.)

(III) seemed most unlikely in view of the known instability, towards acids, of *N*-acylbenziminazoles (cf. Oddo and Ingraffia, *Gazzetta*, 1932, **62**, 1092) and of *N*-(1-hydroxyalkyl)benziminzoles, the latter being in effect substituted aldehyde-ammonias. Structures of type (IV) seemed at first attractive since they would include 5 : 6-dimethyl-1-D-ribitylbenziminazole, a compound bearing a relationship to riboflavin which might be biogenetically significant. Comparison on paper chromatograms showed, however, that the phosphorus-free β-benziminazole is not identical with 5 : 6-dimethyl-1-D-ribitylbenziminazole. The α-benziminazole is unaffected by periodic acid and so contains no free α-glycol grouping; the β-benziminazole, on the other hand, is oxidised by periodic acid, from which it may be deduced that the α-compound contains the grouping $CH(OH)\cdot CH\cdot O\cdot PO_3H_2$. In this laboratory, a method for the detection of α-glycols on paper chromatograms, based on oxidation with periodic acid followed by a colour reaction with Schiff's reagent (Buchanan, Dekker, and Long, forthcoming publication), has recently been developed. Application of this method to the phosphate-free β-benziminazole showed that its behaviour was exactly analogous to that of the pyrimidine and purine ribonucleosides, the periodate-oxidation product being similar in its colour reaction on paper to that of the dialdehyde formed from the natural nucleosides. In this respect, it differed markedly from both 1-(2 : 3-dihydroxypropyl)-5 : 6-dimethylbenziminazole and 5 : 6-dimethyl-1-D-ribitylbenziminazole, with which the method fails, owing, apparently, to further reaction of the side-chain on periodate oxidation. This anomalous behaviour with periodate has also been observed in the case of riboflavin itself by Dr. H. S. Forrest in this laboratory (private communication); the course of the reaction in this and similar cases is not yet clear and will be investigated as opportunity permits. It appears from these experiments that a linkage of type (IV) with a side-chain of a type analogous to that in riboflavin cannot be present in the benziminazole derivatives obtained from vitamin B_{12}.

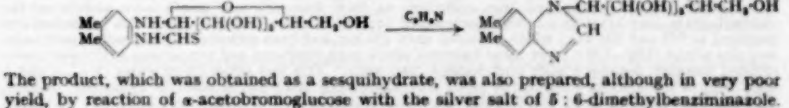
The linkage represented by structure (V) is, of course, glycosidic and we were at first inclined to reject this as a possibility in view of the comparative ease with which *N*-glycosides undergo fission with acids. If the α-benziminazole were a phosphorylated *N*-pentoside or *N*-hexoside of 5 : 6-dimethylbenziminazole its resistance to acids (it appears to be virtually unaffected by 15 hours' heating at 100° with 6N-hydrochloric acid) would seem to be at variance with commonly accepted ideas, the more so as 9-glycosylpurines are easily hydrolysed by dilute acids. Nevertheless, the failure of the α-benziminazole to react with periodate and the reaction of the β-compound to give a product very similar to those obtained from the purine and pyrimidine nucleosides would be most readily explained on the basis of a glycosidic structure in which the α- and β-compounds stand to one another in the same relation as a purine nucleotide to its phosphorus-free nucleoside. It was, therefore, decided to prepare model benziminazole glycosides in order to compare their behaviour towards acid with that of the vitamin degradation products. Both 1-D-glucosyl-5 : 6-dimethylbenziminazole (I; R = $C_6H_{10}O_4$) and 1-D-glucosylbenziminazole (the latter kindly provided by Dr. I. Goodman of the University of Colorado) were unaffected by 20 hours' heating at 100° with 6N-hydrochloric acid and failed to give a Molisch reaction under normal conditions. In these and other respects, the synthetic compounds

closely resembled the β-benziminazole and it seemed almost certain that that they had the same type of structure, *i.e.*, that the α-compound was a benziminazole nucleotide and the β-compound the corresponding nucleoside.

Since this work was carried out, Brink, Holly, Shunk, Peel, Cahill, and Folkers (*J. Amer. Chem. Soc.*, 1950, **72**, 1866) have announced the isolation of 5 : 6-dimethyl-1-D-α-ribofuranosyl-benziminazole (I; R = CH·[CH(OH)]$_3$·CH·CH$_2$·OH) from the hydrolytic degradation of vitamin B_{12} and confirmed the structure by direct comparison with a synthetic specimen. In their paper, Brink *et al.* have suggested that the name ribazole be given to the vitamin B_{12} degradation product 5 : 6-dimethyl-1-α-D-ribofuranosylbenziminazole. We feel that there is little to be gained by the use of such a term; the systematic name of the compound is not unduly complicated. Moreover, the name ribazole is open to strong objection on a variety of grounds; it certainly does not indicate that the compound is a glycoside and the use of a trivial name for a substance which contains two alkyl substituents and a carbohydrate residue (any or all of which might be varied) on the basic nucleus is much to be deplored.

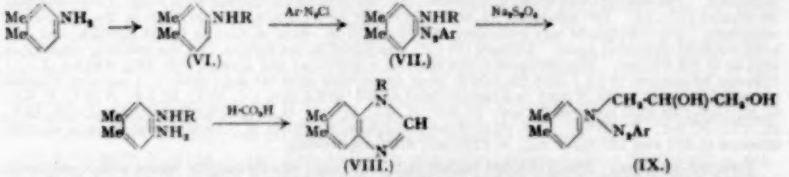
5 : 6-Dimethyl-1-α-D-ribofuranosylbenziminazole is doubtless identical with our β-benziminazole and, if we accept the structure assigned by the Merck group, then other observations can be made on the structure of our phosphorylated benziminazole and of vitamins B_{12} and B_{12a}. The benziminazole nucleotide must have the empirical formula $C_{14}H_{19}O_7N_2P$ and, as it contains no α-glycol grouping, the phosphoryl group must be located at $C_{(2)}$ or $C_{(3)}$ in the ribose residue; its isolation thus determines the position of the phosphorus atom in vitamins B_{12} and B_{12a} (within these limits).

Certain points of chemical interest have arisen from the syntheses of the *N*-substituted benziminazoles. 1-D-Glucopyranosyl-5 : 6-dimethylbenziminazole was prepared by a method similar to that already used in these laboratories for the synthesis of purine glycosides (Baddiley, Lythgoe, and Todd, *J.*, 1944, **318**, and numerous later papers), *viz.*, by the cyclisation of the 2-thioformamidoaniline glucoside:



The product, which was obtained as a sesquihydrate, was also prepared, although in very poor yield, by reaction of α-acetobromoglucose with the silver salt of 5 : 6-dimethylbenziminazole. The scope of the thioformamido-route to benziminazole glycosides is at present under investigation, as are other possible approaches.

The syntheses of 1-(2 : 3-dihydroxypropyl)-5 : 6-dimethylbenziminazole [(VIII); R = CH$_2$·CH(OH)·CH$_2$·OH] and 5 : 6-dimethyl-1-ribitylbenziminazole [VIII; R = CH$_2$·[CH(OH)]$_3$·CH$_2$·OH] were carried out according to the annexed scheme. Under the



conditions employed, the coupling of *N*-(2 : 3-dihydroxypropyl)-o-4-xylidine [VI; R = CH$_2$·CH(OH)·CH$_2$·OH] with 2 : 5-dichlorobenzenediazonium chloride gave a product which appeared to consist mainly of the diazoamino-compound (IX) (cf. Karrer and Meerwein, *Helv. Chim. Acta*, 1936, **19**, 264) which was converted into the isomeric azo-compound [VII; R = CH$_2$·CH(OH)·CH$_2$·OH] on treatment with warm formic acid; the azo-compound was then converted into the benziminazole [VIII; R = CH$_2$·CH(OH)·CH$_2$·OH] as indicated. Attempts to prepare the same benziminazole by hydroxylation of 1-allyl-5 : 6-dimethylbenziminazole were unsuccessful.

Experimental.

Vitamin B_{12c}.—The *vitamin* was provided by Dr. Lester Smith of Glaxo Laboratories Ltd. For analysis, a sample was crystallised repeatedly from aqueous acetone, forming dark red needles (Found, in a sample dried at 100° in a high vacuum: C, 50·5; H, 6·5; N, 13·3; P, 2·05; Co, 4·7. $C_{62}H_{91}O_{15}N_{13}PCo$ requires C, 50·7; H, 6·6; N, 13·1; P, 2·1; Co, 4·0%).

The α-Benziminazole.—(1) *Detection.* Vitamin B_{12} (0·5 mg.; Fantes, Page, Parker, and Lester Smith, *loc. cit.*) was heated under reflux with 8*N*-hydrochloric acid (2 c.c.) and *n*-butanol (2 c.c.) for 70 minutes. After cooling, the contents of the flask were transferred to a small test-tube, and the aqueous layer separated (absorption spectrum: maxima at 277 and 285 mμ.) and evaporated to dryness. The residue was dissolved in a very small drop of water and introduced on to a paper chromatogram. After neutralisation of the spot with ammonia vapour, the chromatogram was irrigated with the top layer of a *n*-butanol–acetic acid–water mixture (4 : 1 : 5; henceforward described as the butanol–acetic acid–water mixture) for 16 hours and, after it had been dried, the paper was photographed in ultra-violet light (cf. Markham and Smith, *Biochem. J.*, 1949, **45**, 294). The R_F value of the single spot in the track of the hydrolysate was 0·55 and that of a 5 : 6-dimethylbenziminazole standard 0·79.

A repeat experiment with parallel hydrolyses of vitamins B_{12} and B_{12c} gave the following spots when photographed as before: vitamin B_{12} hydrolysate, R_F 0·48; vitamin B_{12c} hydrolysate, R_F 0·47; 5 : 6-dimethylbenziminazole standard, R_F 0·77. This paper was used later to demonstrate the presence of the ninhydrin-reacting base in the hydrolysate (below).

(2) *Isolation of the barium salt.* Vitamin B_{12} (146·6 mg.) was heated under reflux with a mixture of concentrated hydrochloric acid (AnalaR; 7 c.c.), water (63 c.c.), and *n*-butanol (10 c.c.) for 2 hours. The solution was cooled, more *n*-butanol (5 c.c.) added, and the butanol layer removed. The pink aqueous layer was extracted twice with butanol (9 c.c.; 7 c.c.) on the steam-bath for 20 minutes each time and the combined dark red butanol extracts were shaken with 2*N*-hydrochloric acid (2 × 10 c.c.). After evaporation of the solvent from the combined aqueous layers under reduced pressure, there remained a red crystalline residue (78 mg.).

Meanwhile, a column of paper pulp for chromatography was prepared by packing the dry paper (H. Reeve Angel and Co. Ltd., London; 40 g.) into a column (20 × 2·5 cm.) and then thoroughly wetting the column with water-saturated *n*-butanol (henceforward described as wet butanol). Metallic ions were removed by introducing two successive solutions of 8-hydroxyquinoline (100 mg.) in wet butanol (4 c.c.). The column was then washed with wet butanol (110 c.c. in all) until free from 8-hydroxyquinoline (no colour with ferric chloride).

The red crystalline hydrolysate was dissolved in a mixture of wet butanol (4 c.c.) and butanol (1 c.c.), the latter being necessary to give a homogeneous solution, which was brought on to the column followed the wet butanol washings (2 × 1 c.c.). Wet butanol was used as the eluant, and the ultra-violet absorption spectra of successive fractions of the eluate were measured in a Beckman spectrophotometer. After 45 c.c. of the eluate had been collected, at least four coloured bands were visible on the chromatogram, and after 75 c.c. the spectrum of the eluate showed the presence of a benziminazole (maxima at 277 and 285 mμ.) which persisted until 155 c.c. had been collected. The leading pink band was also eluted (126—140 c.c.) in these fractions which were combined and evaporated to dryness under reduced pressure, leaving a solid pink residue (34·7 mg.). This was taken up in water (1 c.c.), and a small drop of the solution subjected to paper chromatography using wet butanol for irrigation. A spot, R_F 0·14, was observed when the chromatogram was photographed in ultra-violet light, but no purple spots were obtained on spraying the paper with ninhydrin solution and subsequent heating at 100° (cf. Consden and Gordon, *Nature*, 1948, **162**, 180).

Glacial acetic acid (0·05 c.c.) was added to the remainder of the aqueous solution which was boiled, filtered, and combined with aqueous washings (3 c.c.). Evaporation of the solvent under reduced pressure gave a red gum (30·3 mg.) which was taken up in water (3 c.c.), to which a saturated solution of barium hydroxide was then added dropwise (0·8 c.c. in all) until the solution was alkaline to phenolphthalein. The solution was boiled and filtered, and the precipitate washed with water (1 c.c.) followed by ethanol (10 c.c.). The combined filtrates were boiled for 2 minutes and set aside in the refrigerator overnight. The precipitate was separated and dissolved in water (5 c.c.) as far as possible, and any solid material separated again. Ethanol (10 c.c.) was added to the filtrate, and the resulting suspension kept at 0° for 6 hours. The precipitate was spun off (centrifuge) and washed with 75% ethanol (5 c.c.) followed by acetone (5 c.c.), and the faintly pink amorphous solid (19 mg.) dried in a vacuum at room temperature for 16 hours (Found, in a sample dried at 110° at 0·1 mm.: C, 33·1; H, 3·9; N 5·1; P 6·7; $C_{14}H_{11}O_7N_4PBa,H_2O$ requires C, 32·9; H, 3·7; N, 5·5; P, 6·1. $C_{11}H_{13}O_6N_3PBa,H_2O$ requires C, 33·3; H, 3·9; N, 5·2; P, 5·7%). The ultra-violet absorption spectrum in 0·1*N*-hydrochloric acid showed maxima at 277 and 285 mμ.; $\varepsilon_{max.} = 6730$ and 6360 respectively.

Periodate oxidation. Finely divided barium salt (1·428 mg.) was thoroughly mixed with *N*-sulphuric acid (0·1 c.c.) and water (0·2 c.c.) to precipitate barium sulphate. Sodium metaperiodate (1 c.c.; 0·024*M*.) was added and the mixture set aside with exclusion of light for 20 hours. Determination of the unchanged metaperiodate iodometrically, after neutralisation of the solution with *N*-sodium hydroxide (0·1 c.c.), showed that none had reacted with the α-benziminazole. A similar experiment with the barium salt of cytidine 5′-phosphate (1·938 mg.) (Michelson and Todd, *J.*, 1949, 2476) showed that 1·24 mols. of metaperiodate were consumed per mol. of nucleotide.

The β-Benziminazole.—Detection. Vitamin B_{12} (17·7 mg.) was heated at 100° in a sealed tube with 8*N*-hydrochloric acid for 48 hours and the purple solution so obtained evaporated to dryness. The solid residue was extracted with acetone (3 c.c.) which removed the purple pigment, and the colourless residue was dissolved in wet butanol (3 c.c.) and brought on to a cellulose chromatogram (15·5 × 1·7 cm.; from

17 g. of cellulose and 40 c.c. of wet butanol, heavy metals being removed with 8-hydroxyquinoline as before). Wet butanol was passed through the column, and the ultra-violet absorption spectra of successive 1-c.c. fractions were measured. The benziminazole fraction (from 23 c.c. to 36 c.c. of the eluate) was treated with 8N-hydrochloric acid (0·06 c.c.) and evaporated to dryness in a vacuum, the solid residue was dissolved in water (1 c.c.) and filtered, and the combined filtrate and washings (2 × 0·5 c.c.) were evaporated to dryness. The residue was again taken up in water (0·09 c.c.), and one drop of this solution was subjected to paper chromatography, after neutralisation with ammonia, using the butanol–acetic acid–water mixture as solvent. Two spots were present in the ultra-violet photograph, having R_F values 0·46 and 0·67, the former being due to the α-benziminazole (5 : 6-dimethylbenziminazole standard had R_F 0·77). The R_F value for the α-benziminazole is very sensitive to slight changes in the composition of the butanol–acetic acid–water solvent. In a second chromatogram with wet butanol as solvent, the two spots from the hydrolysate had R_F values 0·12 and 0·78, and 5 : 6-dimethylbenziminazole had R_F 0·89. No ninhydrin-reacting compounds were detected on these chromatograms.

In a similar hydrolysis of vitamin B_{12a} at 100° with 8N-hydrochloric acid for 36 hours, the product was treated exactly as in the previous experiment. The two spots in the track of the hydrolysate had R_F values 0·56 (α-benziminazole) and 0·73, that of 5 : 6-dimethylbenziminazole being 0·79, and the single spot on the same chromatogram from a hydrolysis of vitamin B_{12} with N-hydrochloric acid had R_F 0·55.

The various spots on the above chromatograms were cut out and extracted with water (2 c.c.) for 10 minutes, and the ultra-violet absorption spectra of the solutions determined. The α- and β-benziminazoles showed maxima at 277 and 285 mμ., and unsubstituted 5 : 6-dimethylbenziminazole at 275—276 and 283—284 mμ.

5 : 6-Dimethylbenziminazole.—Vitamin B_{12} (1·1 mg.) was hydrolysed with 6N-hydrochloric acid in a sealed tube at 145° for 16 hours. The purple solution, after evaporation to dryness under reduced pressure, was extracted with acetone (1 c.c.), and the colourless residue, in the minimum quantity of water, transferred to a paper chromatogram. Vitamin B_{12a} (1·1 mg.) was treated similarly. The chromatogram was developed with the butanol–acetic acid–water mixture and photographed as before. Each hydrolysate showed a single spot : vitamin B_{12} hydrolysate, R_F 0·75 ; vitamin B_{12a} hydrolysate, R_F 0·74 ; 5 : 6-dimethylbenziminazole standard, R_F 0·74.

In another experiment, vitamin B_{12a} (0·9 mg.) was heated with 6N-hydrochloric acid (1 c.c.) at 147° for 5 hours, and the colourless fraction isolated in the same way as previously. Paper chromatography as before showed the presence of a single benziminazole, R_F 0·80 (5 : 6-dimethylbenziminazole standard, R_F 0·78). The benziminazole spot from the vitamin B_{12a} hydrolysis was extracted with N-hydrochloric acid (2 c.c. for 30 minutes), and the absorption spectrum of the extract was shown to exhibit maxima at 275 and 283 mμ.

Examination of the α- and the β-Benziminazole by Paper Chromatography.—The α-benziminazole was obtained from the hydrolysis of vitamin B_{12a} (4·9 mg.) with N-hydrochloric acid (colourless residue dissolved in 0·11 c.c. of water), and a mixture of α- and β-benziminazoles was obtained from the hydrolysis of vitamin B_{12} (17·7 mg.) with 8N-hydrochloric acid, subsequent purification being as described above (colourless residue dissolved in 0·09 c.c. of water)

(1) *Presence of phosphorus in the α-benziminazole.* The mixture of the α- and the β-benziminazole after exposure to ammonia vapour was chromatographed on paper by the ascending technique (Williams and Kirby, *Science*, 1948, **107**, 481), with N-butanol as solvent, and photographed in ultra-violet light. The observed R_F values of the two spots, 0·12 and 0·78, corresponded to the α- and the β-compound respectively, and that of a 5 : 6-dimethylbenziminazole standard was 0·89. The paper was then sprayed with the molybdate–perchloric acid reagent of Hanes and Isherwood (*Nature*, 1949, **164**, 1107), heated at 90° for 7 minutes, exposed to water vapour, and finally treated with hydrogen sulphide. A blue spot, indicating the presence of phosphorus, was obtained with R_F 0·12.

(2) *Reaction of the α-benziminazole with sodium metaperiodate.* The α-benziminazole solution (0·015 c.c.) was mixed with an equal volume of sodium metaperiodate solution (0·24M.) on a small watch-glass, and the covered vessel kept in the dark for 20 hours. Water (0·02 c.c.) and glycerol (0·02 c.c.) were added, and the mixture was kept for a further 5 hours. The residue was transferred to a paper chromatogram and developed with the butanol–acetic acid–water mixture. Ultra-violet photography showed two spots, having R_F 0·09 and 0·54 (α-benziminazole standard 0·51), of which the former, after extraction with water, showed no specific absorption in the region 270—300 mμ. characteristic of the benziminazole nucleus. This slow-moving spot was probably caused by the attack of periodate on the filter-paper or by glycerol oxidation products. Examination of the paper for phosphorus showed a single blue spot, having R_F 0·52 (α-benziminazole standard 0·54). The ninhydrin-reactive base present in the original solution (below) was not detectable after the periodate treatment.

(3) *Reaction of the mixed α- and β-benziminazoles with sodium metaperiodate.*—The mixed α- and β-benziminazole solution (0·015 c.c. ; above) was treated with sodium metaperiodate solution (0·24M. ; 0·02 c.c.) as in the previous experiment. Water (0·04 c.c.) and glycerol (0·02 c.c.) were added, and the mixture was kept for a further 24 hours. The resulting solution was subjected to paper chromatography with the butanol–acetic acid–water mixture as solvent, and the dried paper after being photographed in ultra-violet light showed three spots having R_F values, 0·06, 0·50, and 0·94 respectively. The mixed α- and β-benziminazoles, run in parallel for comparison, showed two spots, having R_F values 0·47 and 0·69 respectively. The nature of the slowest-moving spot in the periodate oxidation experiment has been discussed above, where it was shown that this compound does not contain a benziminazole nucleus. The chromatogram was then treated with the phosphate reagent and developed with hydrogen sulphide as described above. The oxidation product gave a single blue spot, of R_F 0·50, and the mixed α- and β-benziminazoles gave a similar blue spot of R_F 0·48 due to the α-compound.

(4) *Use of sodium metaperiodate as a spraying reagent.* A paper chromatogram of the mixed α- and β-benziminazoles was run with the butanol–acetic acid–water mixture as solvent and, after photography in the usual way, the normal two spots were observed, having R_F 0·60 and 0·70 (5 : 6-dimethylbenziminazole standard 0·80). The chromatogram was sprayed with a mixture of equal volumes of 5% sodium metaperiodate solution and 3N-sulphuric acid and kept at room temperature for 30 minutes. It was exposed to sulphur dioxide for 5 minutes in a large beaker, then sprayed with Schiff's reagent (1 g. of rosaniline was dissolved in 80 c.c. of water and the solution just decolorised with sulphur dioxide; the filtered solution was diluted to 1 l.), and again treated with sulphur dioxide to remove the excess of iodine. The paper was kept at room temperature for 24 hours, whereupon a dark blue spot, which intensified with time, appeared at R_F 0·74.

Comparative experiments exactly similar to the above were carried out with a variety of compounds of known structure:

	R_F values of spots observed after ultra-violet photography.	R_F values of dark blue spots obtained after reaction with periodate and Schiff's reagent.
Mixed α- and β-benziminazoles	0·51 (α)	—
	0·68 (β)	0·69
1-(2 : 3-Dihydroxypropyl)-5 : 6-dimethyl-benziminazole	0·71	—
5 : 6-Dimethyl-1-D-ribitylbenziminazole	0·61	—
5 : 6-Dimethylbenziminazole	0·77	—
Mixed α- and β-benziminazoles	0·42	—
	0·63	0·64
Adenosine	0·41	0·39
1-(2 : 3-Dihydroxypropyl)-5 : 6-dimethylbenz-iminazole	0·66	—

The Ninhydrin-reactive Base.—(1) *Detection in the N-hydrochloric acid hydrolysate.* The paper chromatogram of the N-hydrochloric acid hydrolysate of vitamins B_{11} and B_{12} (above), after photography in ultra-violet light to demonstrate the presence of the phosphorylated α-benziminazole, was sprayed with a solution of ninhydrin (0·1%) in *n*-butanol containing 1% of acetic acid. It was then heated at 100° for 5 minutes. The R_F value of the single purple spot in the track of each of the hydrolysates was 0·41.

In a similar chromatogram an alanine standard gave a spot of R_F 0·24; 1-amino-2-propanol and 2-amino-1-propanol after development at 120° for 3 minutes gave spots each of R_F 0·42.

Further chromatograms of the hydrolysate (spots neutralised with ammonia before running of the chromatogram) were carried out as follows: (*a*) In wet butanol with development at 90° for 5 minutes. The base had R_F 0·15. Standards: alanine, 0·06; 1-amino-2-propanol, 0·16; with 2-amino-1-propanol the violet spot appeared only on further heating at 120° for 3 minutes. (*b*) In collidine with development at 120° for 3 minutes: vitamin B_{12} hydrolysate, 0·33; 1-amino-2-propanol, 0·35; 2-amino-1-propanol, 0·37; alanine, 0·14.

(2) *Partial purification.* Vitamin B_{12} (15·9 mg.) was hydrolysed with 8N-hydrochloric acid (5 c.c.) in a sealed tube at 100° for 48 hours. The contents of the tube were removed and evaporated to dryness in a vacuum, and the coloured material was extracted with acetone. The colourless residue was dissolved in wet butanol (2 c.c.), brought on to a column of powdered cellulose (9·5 × 1·7 cm.; 10 g., with heavy metals previously removed by 8-hydroxyquinoline treatment; wet butanol as solvent), and eluted with wet butanol, and successive 10-c.c. fractions were collected. Determination of the ultra-violet absorption of these fractions showed that the first two contained no absorbing material, and that fractions 3—5 inclusive contained material showing absorption maxima at 276 and 285 mμ. These fractions (3—5) were combined, evaporated to dryness, and used in experiments with the mixed α- and β-benziminazoles.

Examination of fractions 1—11 with ninhydrin reagent on paper showed that faint purple colours were given with all of the fractions but that those from fractions 8, 9, and 10 were the most intense. These were, therefore, combined, 8N-hydrochloric acid (0·06 c.c.) being added and the solution evaporated to dryness. The residue was dissolved in water (2 c.c.), any solid material separated, and the solution evaporated to dryness in a high vacuum at room temperature. The crystalline solid (2·6 mg.), which gave a positive Nessler reaction, was dissolved in water (0·1 c.c.), and a portion of the solution used for paper chromatography using the butanol–acetic acid–water mixture as solvent. Treatment of the paper with ninhydrin solution and subsequent heating (90° for 15 minutes) gave a single purple spot, of R_F 0·36, in the track of the hydrolysate. DL-Valine standard, 0·44; DL-leucine standard, 0·60. When fractions 7 and 11 were treated similarly, both residues gave a positive reaction with Nessler's reagent but no colour with ninhydrin after paper chromatography.

The remainder of the solution of the ninhydrin-reactive substance was used in the following experiments:

(3) *Effect of nitrous fumes.* The solution of the ninhydrin-reactive substance (0·015 c.c.) was diluted with water (0·5 c.c.) and nitrous fumes (sodium nitrite—dilute hydrochloric acid) were passed through the solution for 5 minutes. 6N-Hydrochloric acid (1 c.c.) was added and the mixture boiled for 5 minutes. The solution was then taken to dryness in a vacuum, and the residue dissolved in water (0·04 c.c.) and transferred to a paper chromatogram. After development with mixed butanol–acetic acid–water solvent, the chromatogram was dried and treated with ninhydrin solution in the usual way. No

coloured spot was obtained. The R_F value of purple spot from the untreated solution on the same chromatogram was 0·39; cf. DL-alanine, 0·27; DL-valine, 0·48; DL-leucine, 0·64.

(4) *Chromatography on paper pre-treated with copper carbonate.* The solution of the ninhydrin-reactive substance was chromatographed on paper pre-treated with copper carbonate (Crumpler and Dent, *loc. cit.*), with wet butanol as solvent. The chromatogram was sprayed with ninhydrin and heated at 100° for 10 minutes, the R_F value of the single purple spot so obtained being 0·15. A β-alanine standard gave a spot with R_F 0·03, but no coloured spots were obtained from DL-alanine or DL-valine after similar treatment.

N-D-*Monoglucopyranosyl*-4 : 5-*dimethyl*-o-*phenylenediamine*.—4 : 5-Dimethyl-2-nitroaniline was converted into its *N*-D-glucopyranoside in 25% yield by the method of Kuhn and Ströbele (*Ber.*, 1937, **70**, 773).

The glucoside (1·25 g.) was suspended in absolute ethanol (100 c.c.) and hydrogenated in the presence of Raney nickel (0·5 g.) at atmospheric temperature and pressure, until the theoretical volume of hydrogen had been absorbed (7 hours). The colourless product which had largely separated out from the solution was filtered off, together with the catalyst, and extracted from the nickel with cold water (10 c.c.). The pale yellow aqueous solution was used directly for the preparation of the thioformyl derivative (below). The colourless alcoholic mother-liquors from the hydrogenation were taken to dryness at room temperature and gave a faintly yellow solid (180 mg.), m. p. 105—110° (decomp.). This appeared to be fairly stable in air or in absolute ethanol but when dissolved in water, in which it was very soluble, it rapidly darkened. Crystallisation from 80% ethanol caused large losses but yielded small greyish plates, m. p. 105—115° (decomp.) which gave analytical values for N-D-*monoglucopyranosyl*-4 : 5-*dimethyl*-o-*phenylenediamine monohydrate* (Found : C, 53·9; H, 7·7; N, 8·6. $C_{14}H_{22}O_5N_2,H_2O$ requires C, 53·2; H, 7·7; N, 8·9%).

N-D-*Glucopyranosyl*-4 : 5-*dimethyl*-2-*thioformamidoaniline*.—Sodium dithioformate (1 g.) was dissolved in the aqueous solution of diamine obtained as above and the solution kept in a loosely stoppered flask at 20—25° for 52 hours. Hydrogen sulphide was evolved and the solution slowly deposited a mass of small crystals. These were separated, washed with water (1 c.c.) and then ethanol (3 c.c.), and dried in air. The yellowish-grey solid (730 mg.) was stable in air but decomposed with evolution of hydrogen sulphide on being heated to 180°. Crystallisation from ethanol gave the *thioformyl* derivative as small faintly yellow needles, m. p. 180° (decomp.) (Found : C, 52·6; H, 6·8. $C_{15}H_{22}O_5N_2S$ requires C, 52·6; H, 6·4%). The product dissolved readily in boiling water, but hydrogen sulphide was evolved and hydrolysis evidently occurred as 5 : 6-dimethylbenziminazole could be isolated from the solution.

1-D-*Glucopyranosyl*-5 : 6-*dimethylbenziminazole*.—The thioformyl compound (310 mg.) was heated under reflux with anhydrous pyridine (10 c.c.) in an atmosphere of nitrogen for 7 hours, whereafter the evolution of hydrogen sulphide had diminished and the solution had begun to darken. It was cooled and then evaporated to dryness at 30° in a vacuum, and the residual pale brown resin was dissolved in water (1 c.c.). After being kept for 12 hours at room temperature the crystalline product which had formed was separated, washed with cold water (0·5 c.c.), and dried at 100° to a pale grey felted mass (160 mg.), m. p. 165—166°. Recrystallisation from hot water (2·5 c.c.) with charcoal yielded colourless needles (125 mg.), m. p. 166—167° which after air-drying gave analytical figures of 1-D-*glucopyranosyl*-5 : 6-*dimethylbenziminazole sesquihydrate* (Found : C, 53·6; H, 7·2; N, 8·5; loss at 125° over P_2O_5 *in vacuo*, 8·4. $C_{15}H_{20}O_4N_2,1·5H_2O$ requires C, 53·7; H, 6·9; N, 8·4; H_2O, 8·1%). The anhydrous substance was very hygroscopic.

Action of Hydrochloric Acid on 1-D-*Glucopyranosylbenziminazole*.—The glucoside (8·4 mg.) was heated with 6N-hydrochloric acid (2 c.c.) in a sealed tube at 100° for 20 hours. The solvent was removed from the product at room temperature, the gummy residue dissolved in water (0·5 c.c.), and a portion (0·01 c.c.) of the solution used for paper chromatography. A parallel experiment was conducted with the glucoside (8·5 mg.) and N-hydrochloric acid under similar conditions. The chromatogram was developed with wet butanol and finally photographed in ultra-violet light. The various absorbing materials were then extracted from the chromatogram with N-hydrochloric acid (2 c.c. per spot) for 15 minutes and the spectra of the compounds determined :

	R_F value.	Maxima in spectrum ($m\mu$.).
Benziminazole standard	0·84	267, 274
1-D-Glucopyranosylbenziminazole standard	0·49	268, 275
1-D-Glucopyranosylbenziminazole (after 6N-HCl hydrolysis)	0·49	268, 275
1-D-Glucopyranosylbenziminazole (after N-HCl hydrolysis)	0·49	268, 275

Action of Hydrochloric acid on 1-D-*Glucopyranosyl*-5 : 6-*dimethylbenziminazole*.—The glucoside was hydrolysed with 6N-hydrochloric acid in a sealed tube at 100° for 20 hours and the reaction product treated exactly as described in the previous experiment :

	R_F value.	Maxima in spectrum ($m\mu$.).
5 : 6-Dimethylbenziminazole standard	0·87	274—275; 283
1-D-Glucopyranosyl-5 : 6-dimethylbenziminazole standard	0·60	276—277; 285
1-D-Glucopyranosyl-5 : 6-dimethylbenziminazole (after 6N-HCl hydrolysis)	0·60	276—277; 285

5 : 6-*Dimethyl*-1-D-*ribitylbenziminazole* (with Dr. H. S. Forrest).—4 : 5-Dimethyl-2-(D-ribitylamino)-azobenzene (2 g.; Bergel, Cohen, and Haworth, *J.*, 1945, 165) in ethanol (100 c.c.) was reduced by addition of saturated sodium dithionite solution until all the colour had disappeared. The solution was

then evaporated to dryness and the residue thoroughly extracted with alcohol. The solvent was removed from the extracts, and the residue treated with formic acid (98%; 4 c.c.) and 4*N*-hydrochloric acid and heated under reflux for 30 minutes. The resulting solution was cooled, filtered, and neutralised with concentrated ammonia solution, and the yellow precipitate so obtained crystallised from very dilute alcohol to give colourless needles (0·5 g.) of 5 : 6-*dimethyl*-1-D-*ribitylbenziminazole*, m. p. 194—196°, raised to 198—200° by recrystallisation from water (Found : C, 59·6; H, 7·1; N, 10·1. $C_{16}H_{26}O_4N_2$ requires C, 60·0; H, 7·1; N, 10·0%). Light absorption : (i) in water : maxima at 251 and 278 mμ.; $\varepsilon_{max.}$ = 5500 and 6040; (ii) in 0·1*N*-hydrochloric acid : Maxima at 276·5 and 285 mμ.; $\varepsilon_{max.}$ = 7800 and 7450.

N-(2 : 3-*Dihydroxypropyl*)-*o*-4-*xylidine* [VI; R = CH_2·$CH(OH)$·CH_2·OH].—A solution of potassium hydroxide (3 g.) in absolute ethanol (15 c.c.) was added to *o*-4-xylidine (6 g.) and α-monochlorohydrin (5·5 g.) in ethanol (15 c.c.), and the mixture kept overnight at room temperature. The precipitated salt was separated and washed, and the combined filtrates and washings were evaporated to dryness in a vacuum. Dilute sodium hydroxide solution was added to the residue, a brown oil being precipitated. Benzene (10 c.c.) and light petroleum (20 c.c.; b. p. 60—80°) were added, the mixture was well cooled and emulsified, and crystallisation, induced by scratching, was completed at 0° overnight. The *product* (5·2 g.) had m. p. 97—99°, raised to 100—101° by recrystallisation from water (Found : C, 68·0; H, 8·8. $C_{11}H_{17}O_2N$ requires C, 67·7; H, 8·7%).

N-(2 : 5-*Dichlorobenzeneazo*)-*N*-(2 : 3-*dihydroxypropyl*)-*o*-4-*xylidine* (IX).—A clear diazonium solution prepared from 2 : 5-dichloroaniline (3·3 g.) and sodium nitrite (1·7 g.) was added quickly to a stirred solution of *N*-(2 : 3-dihydroxypropyl)-*o*-4-xylidine in acetic acid (100 c.c. of 10%). A gummy material was precipitated from the red solution and after 15 minutes at room temperature, the excess of sodium acetate and the granular orange-red solid were collected, triturated with cold water, washed, and dried (6·2 g.). The *amino-azo*-compound crystallised from dilute alcohol or benzene to give very pale orange felted needles, m. p. 135—136° (decomp. *ca.* 160° with effervescence) (Found : C, 55·1; H, 5·2. $C_{17}H_{18}O_2N_2Cl_2$ requires C, 55·4; H, 5·2%). The product was largely unchanged on treatment with alcoholic sodium dithionite.

1-(2 : 3-*Dihydroxypropyl*)-5 : 6-*dimethylbenziminazole* [VIII; R = CH_2·$CH(OH)$·CH_2·OH].—The above diazoamino-compound (IX) (5·2 g.) was dissolved in hot ethanol (40 c.c. of 75%), and formic acid (10 c.c. of 85%) added. The red solution was cooled and after 3½ hours the product was precipitated by dilution with water and separated after being kept overnight, forming red needles (3·5 g.), m. p. 130—140°, of the crude amino-azo-compound [VII; R = CH_2·$CH(OH)$·CH_2·OH]. This material was dissolved in boiling alcohol and treated with sodium dithionite solution (8 g. in 30 c.c. of water, added in two portions). Inorganic salts were separated from the pale orange solution, and the alcohol was removed from the filtrate in a vacuum. The separated 2 : 5-dichloroaniline was extracted with benzene–light petroleum (1 : 1), and the aqueous solution taken to dryness in a vacuum. The residue was extracted with hot alcohol (3 × 10 c.c.), and the solvent removed from the combined extracts. The residual solid was then dissolved in formic acid (8 c.c. of 85%) containing concentrated hydrochloric acid (2 c.c.), and the solution boiled for 30 minutes. The formic acid was removed *in vacuo* and the residue made alkaline with dilute sodium hydroxide and cooled in the refrigerator. The solid which separated was washed with benzene–light petroleum and then dissolved in boiling water (20 c.c.), and the solution clarified with charcoal. The solution on cooling deposited almost colourless needles of 1-(2 : 3-*dihydroxypropyl*)-5 : 6-*dimethylbenziminazole monohydrate* (0·5 g.) which were purified by recrystallisation from water, then having m. p. 95—98° with resolidification and re-melting at 151—152° (Found : loss on drying at 100° in a vacuum, 7·1. $C_{12}H_{16}O_2N_2,H_2O$ requires 7·6%) (Found, on anhydrous material : C, 65·8; H, 7·0; N, 12·9. $C_{12}H_{16}O_2N_2$ requires C, 65·5; H, 7·3; N, 12·7%).

1-*Allylbenziminazole*.—(1) *From potassium benziminazole*. Benziminazole (3·5 g.) was added to a solution of potassium hydroxide (1·7 g.) in ethanol (25 c.c.), and freshly distilled allyl bromide (3·6 g.) added to the mixture and shaken vigorously. A rapid exothermic reaction occurred and solid was precipitated after a few seconds. After 2 hours, the potassium bromide was separated and washed with alcohol. The filtrate and washings were evaporated to dryness under reduced pressure, the oily product extracted from the residue with ether, and after removal of the solvent the residual brown viscous oil was distilled and the fraction of b. p. 99—100°/0·1 mm. (3·5 g.) collected as a pale yellow oil. The *picrate* formed needles, m. p. 175·5—177° (decomp.), from ethoxyethanol (Found : C, 49·6; H, 3·2. $C_{16}H_{13}O_7N_5$ requires C, 49·6; H, 3·4%).

(2) *From silver benziminazole*. Benziminazole (2 g.) was dissolved in ethanol (40 c.c.) containing aqueous ammonia (*d* 0·880; 1 c.c.). A slight excess of an aqueous solution of silver nitrate was added and the gelatinous precipitate collected after 2 hours, washed with alcohol, and dried over sulphuric acid in a vacuum. The silver salt (2·2 g., 1 mol.) was ground and suspended in benzene (25 c.c.) and, after a little of the solvent had been distilled off to remove any moisture, allyl bromide (3·6 g., 3 mols.) was added and the mixture heated under reflux for 3 hours. The product was purified as in the previous experiment, to give a pale yellow oil (1·3 g., 83%) which gave a picrate identical with that obtained above.

Attempted hydroxylations of the base with hydrogen peroxide–osmium tetroxide (cf. Mugdan and Young, *J.*, 1949, 2988) or performic acid (cf. Swern *et al.*, *J. Amer. Chem. Soc.*, 1946, **68**, 1504) were unsuccessful.

1-*Allyl*-5 : 6-*dimethylbenziminazole*.—This was prepared from silver 5 : 6-dimethylbenziminazole (0·32 g.) and allyl bromide (0·5 g.) as in the previous experiment. The product was distilled at 0·1 mm. to give a pale yellow oil (0·14 g.) which readily gave a *picrate* as long needles, m. p. 192—193° (decomp.), from ethanol (Found : C, 52·3; H, 3·9. $C_{18}H_{17}O_7N_5$ requires C, 52·1; H, 4·1%).

We are indebted to Glaxo Laboratories, Ltd., for supplying us with vitamins B_{12} and B_{12a} and to Dr. T. H. Jukes of Lederle Laboratories Inc., Pearl River, New York, for further generous gifts of vitamin

B_{12}. Our thanks are offered to Professor L. Ruzicka and Dr. W. Manser of the Technische Hochschule, Zurich, for the analysis of vitamin B_{12}. Grateful acknowledgment is made to the D.S.I.R. for a maintenance grant (to J. G. B.) and to the Australian National University for a scholarship (to J. A. M.).

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, July 4th*, 1950.]

---

553. *The Preparation of Dimethyltetrahydrocarbazoles.*

By G. ANDERSON and NEIL CAMPBELL.

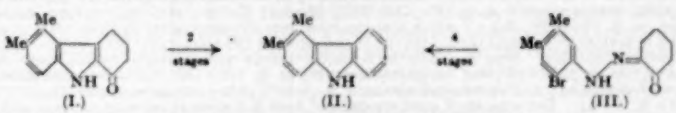
Dimethylcarbazoles are conveniently prepared by Clemmensen reduction of 1-keto-1 : 2 : 3 : 4-tetrahydrocarbazoles, followed by chloranil dehydrogenation of the resulting tetrahydrocarbazoles. The dimethyltetrahydrocarbazoles have a pronounced tendency to form peroxides (cf. Beer *et al.*, *Nature*, 1949, **164**, 362; Campbell and McCall, in the press). Some statements in the literature on the bromination of *o*-4-xylidine are corrected.

COFFEY (*Rec. Trav. chim.*, 1923, **42**, 528) showed that *cyclo*hexane-1 : 2-dione phenylhydrazone, readily prepared by the action of benzenediazonium chloride on 2-hydroxymethylene-*cyclo*hexanone, yields with acids 1-keto-1 : 2 : 3 : 4-tetrahydrocarbazole. Since the keto-group can be reduced to a methylene group (cf. Mears, Oakeshott, and Plant, *J.*, 1934, 272) and the resulting tetrahydrocarbazoles can be smoothly dehydrogenated by chloranil (Barclay and Campbell, *J.*, 1945, 530), a method for the preparation of substituted carbazoles suggests itself.

It was hoped that the carbonyl group of ketotetrahydrocarbazole would enable us to insert alkyl and aryl substituents in the 1-position, but the carbonyl group proved to be quite inert towards Grignard reagents. An explanation of this was sought in chelation between the carbonyl and the imino-group, but must be ruled out since the same inertness occurs in 9-methyl-1-ketotetrahydrocarbazole. The carbonyl group, however, functions normally on Clemmensen reduction (see below).

Attempts to prepare dimethyltetrahydrocarbazoles by the Borsche method or Rogers and Corson's modification thereof (*J. Amer. Chem. Soc.*, 1947, **69**, 2910) were unsatisfactory or unsuccessful. Diazotised xylidines, however, condensed readily with 2-hydroxymethylene-*cyclo*hexanone to give *cyclo*hexane-1 : 2-dione xylylhydrazones, which were readily converted by acids into 1-keto-dimethyltetrahydrocarbazoles and thence by Clemmensen reduction into dimethyltetrahydrocarbazoles. The outstanding feature of the latter substances is the ease with which they combine with a molecule of oxygen when crystallised from light petroleum. These oxygenated substances have a strong green fluorescence in methanol, and peroxide formulæ have been assigned to them (Beer *et al.*, *Nature*, 1949, **164**, 362). Chloranil dehydrogenation of the tetrahydrocarbazoles gave **1** : **2**-, **1** : **4**-, **1** : **3**-, **2** : **3**-, and **3** : **4**-dimethylcarbazoles.

As is to be expected, *o*-4-xylidine gave two ketodimethyltetrahydrocarbazoles, m. p. 201° and 225—227°. These are respectively 1-keto-6 : 7-dimethyl- and 1-keto-5 : 6-dimethyl-carbazole (I) since the latter is converted into **3** : **4**-dimethylcarbazole (II) whose structure follows from its synthesis from *cyclo*hexane-1 : 2-dione 2-bromo-4 : 5-dimethylphenylhydrazone (III) by ring-closure, reduction, dehydrogenation, and dehalogenation.



(I.) (II.) (III.)

The required 5-bromo-*o*-4-xylidine was obtained by the bromination of aceto-*o*-4-xylidide (Mills and Nixon, *J.*, 1930, 2510). There can be little doubt that bromination occurs at the 5-position since the product differs both from the 6-bromo-compound (Crossley and Bartlett, *J.*, 1913, **103**, 1300) and the 3-bromo-compound (Mills and Nixon, *loc. cit.*). However, we have completely failed to substantiate the claim of Jaeger and Blanksma (*Rec. Trav. chim.*, 1906, **25**, 354) that bromination of aceto-*o*-4-xylidide yields the **3** : **6**-dibromo-compound; repeated attempts gave only the above monobromo-product. The results of Jaeger and Blanksma can scarcely be correct, especially since substitution in the 6-position in preference to the 5 is most unlikely (cf. Hinkel *et al.*, *J.*, 1934, 283).

Most carbazoles give a characteristic deep bluish-green colour with sulphuric acid and a drop of nitric acid. It is therefore noteworthy that **1** : **4**- and **3** : **4**-dimethylcarbazole and 1-bromo-**3** : **4**-dimethylcarbazole give only an amber colour with this reagent.

Experimental.

General Procedure.—The methods used are exemplified by the preparation of 1 : 2 : 3 : 4-tetrahydrocarbazole. 2-Hydroxymethylene*cyclo*hexanone and benzenediazonium chloride gave *cyclo*hexane-1 : 2-dione phenylhydrazone, m. p. 183—185° (33%), which afforded 1-keto-1 : 2 : 3 : 4-tetrahydrocarbazole, m. p. 170° (55%), by Coffey's method (*loc. cit.*). The keto-compound was obtained in colourless crystals by running a benzene solution through a column (6" × ¾") of alumina. The keto-compound (1 g.) in the minimum volume of ethanol was added in portions during 3 hours to amalgamated zinc (25 g.) in boiling concentrated hydrochloric acid (7 ml.) and water (3 ml.), further amounts of acid being added portionwise during this time. The mixture was boiled for a further 3 hours, the solution was decanted, the amalgam was washed twice with hot ethanol (5 ml.), and the washings were added to the decanted solution. Addition of water gave a precipitate which was extracted with ether and dried (Na_2SO_4). Evaporation of the ether and crystallisation of the residue from light petroleum (b. p. 100—120°) gave tetrahydrocarbazole, m. p. and mixed m. p. 113—114° (0·5 g.). Chloranil dehydrogenation (Campbell and Barclay, *loc. cit.*) gave an 80% yield of carbazole.

*8-Methyl-*1 : 2 : 3 : 4-*tetrahydrocarbazole.*—*cyclo*Hexane-1 : 2-dione *o*-tolylhydrazone, m. p. 95—96°, gave 1-keto-8-methyl-1 : 2 : 3 : 4-tetrahydrocarbazole, m. p. 166—167° (33%), which on reduction afforded 8-methyl-1 : 2 : 3 : 4-tetrahydrocarbazole, m. p. and mixed m. p. 97—99° (87%) (Found : C, 84·0; H, 8·2. Calc. for $C_{13}H_{15}N$: C, 84·3; H, 8·1%). Crystallisation from light petroleum gave a *peroxide*, m. p. 122° (decomp.) (Found : C, 72·6; H, 7·5. $C_{13}H_{15}O_2N$ requires C, 71·9; H, 6·9%).

Synthesis of 1 : 2-*Dimethylcarbazole.*—cyclo*Hexane*-1 : 2-*dione* o-3-*xylylhydrazone*, deep-red prisms (from light petroleum), m. p. 89—91° (53%) (Found : C, 73·1; H, 7·8. $C_{14}H_{16}ON_2$ requires C, 73·1; H, 7·8%), gave 1-*keto*-7 : 8-*dimethyltetrahydrocarbazole*, needles (from benzene or ethanol), m. p. 200—201° (46%) (Found : C, 79·4; H, 7·0. $C_{14}H_{15}ON$ requires C, 79·5; H, 7·1%), and thence 7 : 8-*dimethyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, plates (from light petroleum), m. p. 84—86° (Found : C, 83·9; H, 8·8; N, 7·2. $C_{14}H_{19}N$ requires C, 84·4; H, 8·5; N, 7·0%). The last-mentioned compound forms a *picrate*, chocolate-coloured needles (from benzene), m. p. 157—158° (Found : N, 13·2. $C_{20}H_{22}O_7N_4$ requires N, 13·1%), and a *peroxide*, m. p. 115° (decomp.) (Found : C, 72·2; H, 7·3. $C_{14}H_{17}O_2N$ requires C, 72·7; H, 7·4%). 1 : 2-*Dimethylcarbazole*, obtained from the tetrahydro-compound as prisms (from light petroleum), m. p. 147—148° (42%) (Found : C, 85·6; H, 6·9. $C_{14}H_{13}N$ requires C, 86·2; H, 6·7%), forms a *picrate*, orange-red needles (from benzene), m. p. 162—163° (Found : N, 13·2. $C_{20}H_{16}O_7N_4$ requires N, 13·2%).

Synthesis of 1 : 4-*Dimethylcarbazole.*—This synthesis involved cyclo*hexane*-1 : 2-*dione* p-*xylylhydrazone*, yellow plates (from methanol), m. p. 71—73° (56%) (Found : C, 72·6; H, 7·8%), 1-*keto*-5 : 8-*dimethyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, needles (from methanol), m. p. 224—225° (54%) (Found : C, 78·7; H, 7·2%), and 5 : 8-*dimethyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, prisms [from aqueous methanol or light petroleum (b. p. 80—100°)], m. p. 88—89° (98%) (Found : C, 84·0; H, 8·0; N, 7·0%), which forms a *picrate*, chocolate-brown needles (Found : N, 13·1%), and a *peroxide*, m. p. 128° (decomp.) (Found : C, 72·7; H, 7·5; N, 6·1%). 1 : 4-*Dimethylcarbazole*, needles (from light petroleum), m. p. 79—82° (yield 52%) (Found : C, 85·3; H, 6·5%), gives a *picrate*, red needles (from benzene), m. p. 142—143° (Found : N, 12·8%).

1 : 3-*Dimethylcarbazole.*—The following were obtained. cyclo*Hexane*-1 : 2-*dione* m-4-*xylylhydrazone*, dark-red prisms (from light petroleum) or orange rhombic prisms (from ethanol), m. p. 81—83° (55%) (Found : C, 72·2; H, 7·7%). 1-*Keto*-6 : 8-*dimethyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, prisms (from methanol), m. p. 191—192° (45%) (Found : C, 78·7; H, 7·0%). 6 : 8-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, prisms (from light petroleum), m. p. 92—94° (72%) (Found : C, 83·7; H, 8·6%), which gives a *picrate*, chocolate-brown needles, m. p. 162—163° (Found : N, 12·6%), and a *peroxide*, m. p. 130° (decomp.) (Found : C, 73·7; H, 7·7; N, 5·9%). 1 : 3-Dimethylcarbazole, prisms, m. p. 94° (26%) (Found : C, 86·1; H, 6·8%), which gives a picrate, bright red needles (from benzene), m. p. 186—187°.

2 : 3- *and* 3 : 4-*Dimethylcarbazole.*—cyclo*Hexane*-1 : 2-*dione* o-4-*xylylhydrazone* (10 g.), yellow plates (from acetic acid or ethanol), m. p. 163—165° (74%) (Found : C, 73·0; H, 7·8%), on ring-closure gave a mixture, m. p. 170—178° (6·5 g.), which was separated into its components by dissolution in a boiling mixture of acetone and glacial acetic acid (2 : 1) and allowing the solution to cool slowly in a stoppered vessel without shaking. After two days the resulting crystals were separated by hand into elongated prisms (*A*), m. p. 196—198°, and compact prisms (*B*), m. p. 175—185°. *A* on recrystallisation gave 1-*keto*-6 : 7-*dimethyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, m. p. 201°, yellow elongated prisms (Found : C, 78·6; H, 7·2; N, 6·7%). The crystals *B* were crystallised from the same mixture of solvents and yielded elongated and compact prisms which were mechanically separated. The former, m. p. 201°, were identical with *A* and the latter after three crystallisations from acetone–glacial acetic acid gave 1-*keto*-5 : 6-*dimethyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, m. p. 225—227° (Found : C, 79·5; H, 7·1%).

6 : 7-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, m. p. 119—130° (yield, 78%) (Found : C, 84·1; H, 8·6; N, 7·0%), gave a *picrate*, chocolate-coloured needles (from benzene), m. p. 168° (Found : N, 13·0%), and on dehydrogenation yielded 2 : 3-*dimethylcarbazole*, plates (from benzene), m. p. 250—252° (42%) (Found : C, 86·2; H, 6·9%). The *picrate* separated from benzene in red needles, m. p. 166—168° (Found : N, 12·6%).

5 : 6-Dimethyl-1 : 2 : 3 : 4-tetrahydrocarbazole was obtained as an oil which on dehydrogenation gave 3 : 4-*dimethylcarbazole*, prisms (from benzene), m. p. 159—160° (Found : C, 85·8; H, 7·1%), which gave no m. p. depression when mixed with 3 : 4-dimethylcarbazole prepared by the method given below.

Synthesis of 3 : 4-*Dimethylcarbazole.*—Bromination of aceto-*o*-4-xylidide in glacial acetic acid gave aceto-5-bromo-*o*-4-xylidide, prisms (from ethanol), m. p. 165—166° (Found : N, 5·5; Br, 32·3. Calc. for $C_{10}H_{12}ONBr$: N, 5·8; Br, 33·0%), which on hydrolysis gave 5-bromo-*o*-4-xylidine, plates [from light

petroleum (b. p. 80—100°)], m. p. 85—87° (Found : Br, 41·0. Calc. for $C_8H_{10}NBr$: Br, 40·0%). The diazotised amine gave by the methods outlined above first cyclo*hexane*-1 : 2-*dione* 5-*bromo*-o-4-*xylylhydrazone*, deep-red prisms (from light petroleum), m. p. 154—156° (Found : N, 8·9; Br, 26·4. $C_{14}H_{15}ON_2Br$ requires N, 9·1; Br, 25·9%), and thence 8-*bromo*-1-*keto*-5 : 6-*dimethyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, colourless prisms, m. p. 211°, after crystallisation first from ethanol–acetic acid and then benzene (Found : N, 4·9; Br, 27·4. $C_{14}H_{14}ONBr$ requires N, 4·8; Br, 27·4%). Clemmensen reduction gave 8-*bromo*-5 : 6-*dimethyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, prisms (from ethanol or light petroleum), m. p. 101° (74%) (Found : Br, 29·5. $C_{14}H_{16}NBr$ requires 28·8%). It forms a *picrate*, reddish-brown needles (from benzene), m. p. 173—174° (Found : N, 11·0. $C_{20}H_{19}O_7N_4Br$ requires N, 11·0%). Attempts to remove the bromine atom by alkali and aluminium–nickel alloy were unsuccessful. Chloranil dehydrogenation yielded 1-*bromo*-3 : 4-*dimethylcarbazole*, which was purified by passing through a column of alumina. A pale yellow band with a blue fluorescence on elution gave the carbazole which crystallised from light petroleum in prisms, m. p. 98—99° (50%) (Found : Br, 29·3. $C_{14}H_{12}NBr$ requires Br, 29·2%). It forms a *picrate*, red needles (from benzene), m. p. 163° (Found : N, 10·3. $C_{20}H_{15}N_4Br$ requires N, 11·1%). The carbazole (0·33 g.), red phosphorus (0·2 g.), and hydriodic acid (*d* 1·96; 5 ml.) were boiled for 4 hours and poured into aqueous potassium iodide solution. After 1 hour the mixture was extracted with ether and the extract shaken in turn with aqueous sodium hydroxide, water, aqueous sodium thiosulphate, and water. Evaporation gave a brown residue which was dissolved in benzene and passed through a column of alumina (3" × 1"). A band with a bright blue fluorescence was eluted and yielded 3 : 4-dimethylcarbazole, prisms [from light petroleum (b. p. 80—100°)], m. p. 150—160° (43%).

UNIVERSITY OF EDINBURGH, KING'S BUILDINGS, EDINBURGH, 9. [*Received, July 4th*, 1950.]

---

554. *The Associating Effect of the Hydrogen Atom. Part XIV. The Structure of Diacylamines and Related Substances.*

By LOUIS HUNTER and NORMAN G. REYNOLDS.

Measurement of molecular weight of diacylamines, including acylsulphonyl- and disulphonylamines, by the cryoscopic method indicates a high degree of molecular association in these compounds, but on replacement of the imido-hydrogen atom the association is completely destroyed. The association of the former type is therefore attributed to intermolecular N–H–O bonds; and their tautomeric behaviour is held to be mesohydric (*i.e.*, due to the intermolecular sharing of the tautomeric hydrogen atom) rather than prototropic. Absence of the imidol form in these compounds is also supported by the properties of their metallic derivatives which, unlike those of the β-diketones, are typical non-chelate compounds.

THE main tenet of the conception of "mesohydric tautomerism" is the non-existence of individual tautomers in compounds exhibiting it. Such substances have been shown in previous parts of this series to possess an associated structure in which molecules are held together by intermolecular hydrogen bonds; it is assumed that the hydrogen atoms concerned are shared between adjacent molecules at the alternative sites customary in tautomeric change (Hunter, *J.*, 1945, 806). Crystallographic verification of this assumption is now beginning to accumulate; *e.g.*, acetamide (Senti and Harker, *J. Amer. Chem. Soc.*, **1940**, **62**, 2008), acetanilide (Brown and Corbridge, *Nature*, **1948**, **162**, 72), dicyandiamide (Hughes, *J. Amer. Chem. Soc.*, **1940**, **62**, 1258), melamine (*idem*, *ibid.*, **1941**, **63**, 1737), and the amino-pyrimidines (Clews and Cochran, *Acta Crystall.*, **1948**, **1**, 4; **1949**, **2**, 46) have all been shown to possess structures in which the molecules are juxtaposed in the crystal in such a way that the bonded hydrogen atom is shared between the alternative tautomeric sites in adjacent molecules. On the other hand, substances whose tautomeric behaviour depends on hydrogen attached to carbon, owing to the inability of the CH group to take part in stable hydrogen-bond formation, are non-associated and exist as individual tautomers interconvertible by a prototropic mechanism.

Acceptance of the theory of mesohydric tautomerism would therefore require the abandonment of the implications usually formulated as the reversible equilibrium $\cdot CO\cdot NH\cdot \rightleftharpoons \cdot C(OH){:}N\cdot$ in describing the tautomeric amide system, and of corresponding equilibria for all other mesohydric tautomeric systems. Support for this view is now sought in a comparison of compounds owing their tautomeric behaviour to the CH group (prototropic) with those owing it to the NH group (mesohydric). In particular, the β-diketones and the β-keto-esters (keto–enol type) will be compared with the diacylamines (amide–imidol type), and Table I compares the boiling points (at atmospheric pressure) of pairs of substances possessing on the one hand the group $\cdot CO\cdot CH_2\cdot CO\cdot$ and on the other the group $\cdot CO\cdot NH\cdot CO\cdot$, together with their methyl derivatives. It is noteworthy that, in spite of a difference of only one unit in formal molecular weight (expressed in parentheses), not only are the boiling points of the former type much lower than those of the latter, but the effect of methylating the tautomeric hydrogen atom is generally

TABLE I.

		B. p.			B. p.
$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CO_2Et$	(130)	181°	$CH_3{\cdot}CO{\cdot}NH{\cdot}CO_2Et$ (131)		205—215°
$CH_3{\cdot}CO{\cdot}CHMe{\cdot}CO_2Et$	(144)	186	$CH_3{\cdot}CO{\cdot}NMe{\cdot}CO_2Et$ (145)		189
$CH_3{\cdot}CO{\cdot}CMe_2{\cdot}CO_2Et$	(158)	185			
$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CH_3$	(100)	139	$CH_3{\cdot}CO{\cdot}NH{\cdot}CO{\cdot}CH_3$ (101)		223
$CH_3{\cdot}CO{\cdot}CHMe{\cdot}CO{\cdot}CH_3$	(114)	169	$CH_3{\cdot}CO{\cdot}NMe{\cdot}CO{\cdot}CH_3$ (115)		192
$CH_3{\cdot}CO{\cdot}CMe_2{\cdot}CO{\cdot}CH_3$	(128)	174			
$CO_2Et{\cdot}CH_2{\cdot}CO_2Et$	(160)	198	$CO_2Et{\cdot}NH{\cdot}CO_2Et$ (161)		226
$CO_2Et{\cdot}CHMe{\cdot}CO_2Et$	(174)	199			
$CO_2Et{\cdot}CMe_2{\cdot}CO_2Et$	(188)	196			

to raise the boiling points of the former type but substantially to lower those of the latter. These effects are in harmony with the conclusion that substances possessing the group ·CO·NH·CO· are associated by a hydrogen-bond mechanism, whilst those possessing the group ·CO·CH_2·CO· are not. The unimolecular character of the latter type has been demonstrated by von Auwers (*Z. physikal. Chem.*, **1893**, **12**, 692; **1894**, **15**, 33), and this together with the other physical and chemical properties of the β-diketones is in complete accord with their representation as the following equilibrium :

(I.)

Indeed, the quantitative assessment of this equilibrium and its mobility under the influence of catalysts have provided the very basis for the development of tautomeric theory in the last half-century. Nevertheless, in spite of the abundant proof of prototropy in the case of keto–enol systems, the representation of amides as an amide–imidol equilibrium rests on nothing more secure than an implied analogy. It is true, however, that extensive spectroscopic studies on amides have been made, but owing to the difficulty of interpretation of spectroscopic data the evidence is largely conflicting. Hantzsch (*Ber.*, **1931**, **64**, 661) claimed that the ultra-violet absorption spectra of trichloroacetamide and benzamide point to a predominantly imidol structure in these amides, but Freymann and Freymann (*Compt. rend.*, **1936**, **202**, 1850) found nothing in the infra-red absorption spectra of benzamide and other amides to correspond to the hydroxyl group. On the other hand, recent measurements of ultra-violet absorption of diacetylamine (Polya and Spotwood, *Rec. Trav. chim.*, **1949**, **68**, 573) are interpreted as favouring an imidol–enol structure. A detailed examination of infra-red absorption of a large number of amides by Richards and Thompson (*J.*, **1947**, 1248) indicated the absence of the C=N link and therefore of the imidol structure. Their conclusions favour the formal amide structure with intermolecular N–H–O bonds, a result which is in harmony with *X*-ray diffraction evidence for crystalline acetamide (Senti and Harker, *loc cit.*).

For the purpose of the present investigation, measurements of molecular weight of a large number of imido-compounds containing two acyl (or other electron-attracting) groups have been made, and the results indicate a high degree of molecular association in these compounds. Figs. 1—6 show the variation of the association factor (α) with concentration in nitrobenzene or benzene solution, molecular weights being measured cryoscopically. The choice of nitrobenzene as a cryoscopic solvent has been made necessary by the sparing solubility of many of the solutes; that such solutes continue to exhibit molecular association in this donor solvent is held to give additional support to the view that they possess a highly associated structure. As in previous parts of this series, molecular association is inferred in all cases in which the association factor increases substantially with rising concentration; *i.e.*, a steep association–concentration curve is taken to indicate molecular association, whereas a flat or gently sloped curve (in the region, $\alpha = 1$) is interpreted as indicating the absence of association. It will be seen from Fig. 1 (showing acylcarbamic esters, diacylamines, and dicarbalkoxyamines), Fig. 2 (showing acylsulphonamides), Fig. 3 (showing disulphonylamines), and Fig. 4 (showing acylthiocarbamic esters), that the compounds possessing an unsubstituted imido-group are all highly associated, but that substitution of the imido-hydrogen atom by alkyl or aryl groups causes complete suppression of molecular association. It would appear, then, that the molecular association of the former type is due to intermolecular hydrogen bonding (N–H–O) of

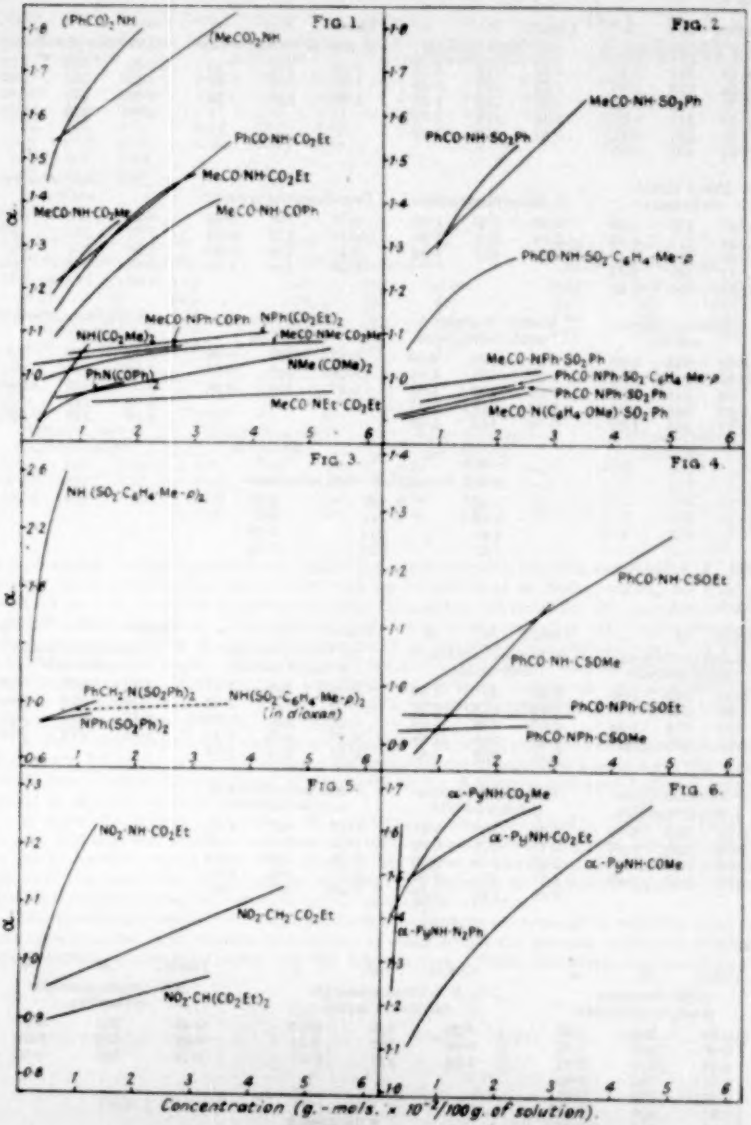


FIG. 1.
(PhCO)$_2$NH
(MeCO)$_2$NH
PhCO·NH·CO$_2$Et
MeCO·NH·CO$_2$Et
MeCO·NH·CO$_2$Me
MeCO·NH·COPh
MeCO·NPh·COPh
NPh(CO$_2$Et)$_2$
NH(CO$_2$Me)$_2$
MeCO·NMe·CO$_2$Me
NMe(COMe)$_2$
PhN(COPh)$_2$
MeCO·NEt·CO$_2$Et
FIG. 2.
MeCO·NH·SO$_2$Ph
PhCO·NH·SO$_2$Ph
PhCO·NH·SO$_2$·C$_6$H$_4$Me-p
MeCO·NPh·SO$_2$Ph
PhCO·NPh·SO$_2$·C$_6$H$_4$Me-p
PhCO·NPh·SO$_2$Ph
MeCO·N(C$_6$H$_4$OMe)·SO$_2$Ph
FIG. 3.
NH(SO$_2$·C$_6$H$_4$Me-p)$_2$
PhCH$_2$·N(SO$_2$Ph)$_2$
NH(SO$_2$·C$_6$H$_4$Me-p)$_2$ (in dioxan)
NPh(SO$_2$Ph)$_2$
FIG. 4.
PhCO·NH·CSOEt
PhCO·NH·CSOMe
PhCO·NPh·CSOEt
PhCO·NPh·CSOMe
FIG. 5.
NO$_2$·NH·CO$_2$Et
NO$_2$·CH$_2$·CO$_2$Et
NO$_2$·CH(CO$_2$Et)$_2$
FIG. 6.
α-PyNH·CO$_2$Me
α-PyNH·CO$_2$Et
α-PyNH·COMe
α-PyNH·NPh
α
Concentration (g.-mols. × 10^{-2}/100 g. of solution).

Fig. 1.

Concn.	*M.*	a.
NN-Dibenzoylamine.		
0·36	331	1·47
0·54	329	1·46
0·74	365	1·62
1·15	377	1·67
1·54	384	1·71
2·05	405	1·80

Concn.	*M.*	a.
NN-Diacetylamine.		
0·55	*156*	*1·55*
1·14	*161*	*1·59*
1·85	*169*	*1·67*
2·56	*172*	*1·71*
3·67	*185*	*1·83*

Concn.	*M.*	a.
Methyl acetylcarbamate.		
0·53	140	1·19
1·02	150	1·28
1·68	159	1·36

Concn.	*M.*	a.
Ethyl benzoylcarbamate.		
0·67	236	1·22
1·53	252	1·30
2·66	277	1·44
3·50	294	1·52

Ethyl acetylcarbamate.		
0·57	*150*	*1·14*
1·38	*171*	*1·30*
1·98	*182*	*1·35*
2·53	*187*	*1·43*
2·83	*190*	*1·45*

N-Benzoylacetamide.		
0·60	178	1·09
2·10	212	1·30
3·33	228	1·40

Dicarbomethoxyamine.		
0·16	106	0·80
0·47	126	0·95
0·81	134	1·00
1·06	140	1·05

NN-Dicarbethoxyaniline.		
0·91	249	1·05
1·77	252	1·07
2·80	254	1·07
3·62	259	1·09
4·20	261	1·10

N-Benzoylacetanilide.		
0·21	243	1·02
0·59	247	1·03
1·24	248	1·04
1·97	252	1·05
2·77	256	1·07

Methyl *N*-acetyl-*N*-methylcarbamate.		
0·45	129	0·99
1·26	136	1·04
2·06	134	1·02
3·66	140	1·07
5·10	142	1·08

NN-Dibenzoylaniline.		
0·37	269	0·90
1·26	292	0·97
1·81	295	0·98

NN-Diacetylmethylamine.		
0·64	*109*	*0·95*
1·85	*111*	*0·97*
3·51	*118*	*1·03*
4·09	*119*	*1·04*
5·39	*121*	*1·06*

Concn.	*M.*	a.
Ethyl *N*-acetyl-*N*-ethylcarbamate.		
1·32	*147*	*0·93*
3·42	*154*	*0·97*
4·48	*152*	*0·96*
5·37	*150*	*0·94*

Fig. 2.

Concn.	*M.*	a.
N-Benzoylbenzenesulphonamide.		
1·01	345	1·32
1·36	365	1·40
1·80	376	1·44
2·34	398	1·53

Concn.	*M.*	a.
N-Benzenesulphonylacetamide.		
0·81	257	1·29
1·48	275	1·38
2·05	286	1·44
2·80	306	1·54
3·47	323	1·63

Concn.	*M.*	a.
N-Benzoyltoluene-*p*-sulphonamide.		
0·54	294	1·07
0·89	322	1·17
1·41	331	1·20
1·87	342	1·25
2·26	353	1·28

Concn.	*M.*	a.
N-Benzenesulphonylacetanilide.		
0·46	267	0·97
1·16	273	0·99
2·47	279	1·01
2·78	279	1·01

N-Benzoyltoluene-*p*-sulphonanilide.		
0·72	333	0·95
1·12	333	0·95
1·79	340	0·97
2·22	346	0·99

N-Benzoylbenzenesulphonanilide.		
0·19	305	0·91
0·79	311	0·92
1·24	318	0·94
1·74	324	0·96
2·40	330	0·98

N-Benzenesulphonylacet-*p*-anisidide.		
0·43	277	0·91
0·90	276	0·91
1·33	289	0·95
1·79	286	0·94
2·48	297	0·97

Fig. 3.

Concn.	*M.*	a.
NN-Ditoluene-*p*-sulphonylamine.		
0·29	442	1·36
0·27	600	1·85
0·49	717	2·21
0·61	763	2·35
0·76	835	2·57
0·87	309	0·95
1·93	314	0·97
2·83	317	0·97
3·55	321	0·99

* In dioxan.

Concn.	*M.*	a.
NN-Dibenzenesulphonylbenzylamine.		
0·39	335	0·87
0·85	362	0·94
1·25	377	0·97

Concn.	*M.*	a.
NN-Dibenzenesulphonylaniline.		
0·46	323	0·87
0·71	333	0·89
1·19	346	0·93

Fig. 4.

Concn.	*M.*	α.	Concn.	*M.*	α.	Concn.	*M.*	α.	Concn.	*M.*	α.
Ethyl benzoylthion-carbamate.			Methyl benzoylthion-carbamate.			Methyl *N*-benzoyl-*N*-phenylthioncarbamate.			Ethyl *N*-benzoyl-*N*-phenylthioncarbamate.		
0·57	*211*	*1·01*	*0·58*	*169*	*0·87*	*0·33*	*250*	*0·92*	*0·41*	*271*	*0·95*
1·20	*212*	*1·01*	*1·16*	*183*	*0·94*	*1·47*	*252*	*0·93*	*1·13*	*270*	*0·95*
1·91	*223*	*1·07*	*1·65*	*195*	*1·00*	*2·54*	*252*	*0·93*	*1·96*	*271*	*0·95*
2·63	*233*	*1·11*	*2·49*	*211*	*1·08*				*2·62*	*272*	*0·95*
3·51	*245*	*1·17*	*2·92*	*221*	*1·14*				*3·26*	*272*	*0·95*
4·39	*255*	*1·22*									
5·01	*263*	*1·26*									

Fig. 5.

Concn.	*M.*	α.	Concn.	*M.*	α.	Concn.	*M.*	α.
Ethyl nitrocarbamate.			Ethyl nitroacetate.			Ethyl nitromalonate.		
0·20	*127*	*0·95*	*0·55*	*128*	*0·96*	*0·51*	*184*	*0·90*
0·47	*140*	*1·05*	*1·25*	*129*	*0·97*	*1·44*	*187*	*0·91*
0·78	*150*	*1·12*	*2·13*	*135*	*1·01*	*2·34*	*195*	*0·95*
1·05	*156*	*1·17*	*3·54*	*144*	*1·08*	*3·28*	*199*	*0·97*
1·29	*164*	*1·23*	*4·66*	*150*	*1·13*			

Fig. 6.

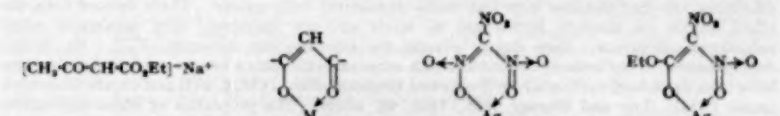
Concn.	*M.*	α.	Concn.	*M.*	α.	Concn.	*M.*	α.	Concn.	*M.*	α.
2-Phenyldiazo-aminopyridine.			Methyl 2-pyridyl-carbamate.			Ethyl 2-pyridyl-carbamate.			2-Acetamido-pyridine.		
0·18	*245*	*1·24*	*0·25*	*216*	*1·42*	*0·49*	*236*	*1·49*	*0·43*	*151*	*1·11*
0·24	*291*	*1·47*	*0·66*	*237*	*1·56*	*1·23*	*258*	*1·56*	*1·29*	*175*	*1·28*
0·28	*318*	*1·60*	*1·16*	*242*	*1·59*	*2·13*	*268*	*1·61*	*2·31*	*192*	*1·41*
			1·40	*253*	*1·66*	*2·81*	*278*	*1·66*	*3·21*	*204*	*1·50*
									4·70	*228*	*1·66*

a kind similar to that suggested for amides and sulphonamides (Chaplin and Hunter, *J.*, 1937, 1114). Such a structure is inconsistent with the formation of an imidol, which, by analogy with the enol (I), would be expected to assume the chelate ring structure (II), and thus to show non-associating behaviour. Similar associated character is revealed in ethyl nitrocarbamate, which is compared (Fig. 5) with the unassociated nitroacetate and nitromalonate; and Fig. 6 illustrates the high degree of association in the acyl-, carbalkoxy-, and aryldiazo-derivatives of 2-aminopyridine. The molecular association of all these compounds indicates that they possess *intermolecular* N–H–O or N–H–N bonds, structures completely at variance with the chelate ring structures (V), (VI), and (VII).

A list of the diacylamines and related substances on which measurements have been made is shown in Table II; in the third column are indicated the hypothetical tautomers which would result from prototropic change, all of which, by virtue of their co-ordinated hydroxyl groups, would be expected to be non-associated.

In spite of the highly associated character of the substances listed in Table II it could be argued that this is no proof of the absence in such systems of the imidol form, which, if present in small amounts, would have little effect on the degree of association measured in solution. To meet this valid point a comparison has been made between the metallic derivatives of some diacylamines and those derived from certain prototropic systems.

(1) *Metallic Derivatives of Prototropic Systems.*—Prototropic systems in which at least one tautomer is acidic yield metallic derivatives, of which by far the greatest number of examples are provided by the β-diketones and the β-keto-esters. Those containing alkali metals are

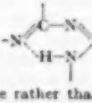


(VIII.) (IX.) (X.) (XI.)

clearly electrovalent salts (*e.g.*, ethyl sodioacetoacetate, VIII), but those derived from metals of high co-ordinative capacity possess properties indicating a structure (IX; M = 1 equiv. of

metal) in which the metal is covalently attached to the two keto-oxygen atoms (Morgan and Moss, *J.*, 1913, **103**, 78; 1914, **105**, 189), a structure which receives support from *X*-ray diffraction evidence (Cox and Webster, *J.*, 1935, 731). Such chelate metallic compounds are derived from and are structurally closely related to the enol (I), and this is doubtless the origin of the ferric chloride colour test for enols. By virtue of the lack of ionic character in the metal M, these derivatives are only sparingly soluble in water, are frequently soluble in organic solvents, and often possess high colour, usually quite different from that of the metallic ion.

TABLE II.

	Imido-compound.	Structural group.	Hypothetical tautomer	
Fig. 1.	Acylcarbamic esters, R·CO·NH·CO_2R Diacylamines, R·CO·NH·COR Dicarbalkoxyamines, CO_2R·NH·CO_2R	·CO·NH·CO·		(II.)
Fig. 2.	Acylsulphonylamines, R·SO_2·NH·COR	·CO·NH·SO_2·		(III.)
Fig. 3.	Disulphonylamines, R·SO_2·NH·SO_2R	·SO_2·NH·SO_2·		(IV.)*
Fig. 4.	Acylthioncarbamic esters, R·CO·NH·CS·OR	·CO·NH·CS·		
Fig. 5.	Nitrocarbamic esters, NO_2·NH·CO_2R	·CO·NH·NO_2		(V.)
Fig. 6.	2-Acylamidopyridines, C_5H_4N·NH·COR 2-Pyridylcarbamic esters, C_5H_4N·NH·CO_2R	·N:C·NH·CO·		(VI.)
	2-Aryldiazoaminopyridines, C_5H_4N·NH·N:NR	·N:C·NH·N:N·		(VII.)

* Recent work on the structure of the sulphone group favours double rather than co-ordinate bonds in these formulæ.

Metallic derivatives of other prototropic systems of similar types are illustrated by silver nitroform (X) (Sidgwick's "Organic Chemistry of Nitrogen," Taylor and Baker, 1942, p. 246) and the silver salt of ethyl dinitroacetate (XI).

(2) *Metallic Derivatives of Diacylamines.*—In spite of being stronger acids than the β-diketones, the diacylamines form less stable derivatives with metals. Those derived from the alkali metals are strongly hydrolysed by water and are frequently only obtainable under anhydrous conditions; they clearly possess the electrovalent structure (XII). By double decomposition of the sodium derivatives with other metallic salts a few heavy-metal derivatives have been described, such as silver (Barth and Senhofer, *Ber.*, 1876, **9**, 977) and cupric dibenzoylamine (XIII) (Ley and Werner, *ibid.*, 1913, **46**, 4049). The properties of these derivatives suggest a structure similar to that of the sodium salt (XII). For example, the cupric compound (dihydrate) is blue-grey in colour and is fairly easily hydrolysed; it has none of the properties usually associated with co-ordinated copper, and is best represented as (XIII) rather than as a derivative of (II).

In the present investigation only those diacylamines having one or two arylsulphonyl groups have proved sufficiently acidic to yield salts stable enough to be characterised. Some

$[R{\cdot}CO{\cdot}N{\cdot}COR]^-Na^+$ (XII.) $[Ph{\cdot}CO{\cdot}N{\cdot}COPh]^-{}_2Cu^{++},2H_2O$ (XIII.) $CH_3{\cdot}CO{\cdot}NH{\cdot}SO_2{\cdot}C_6H_4{\cdot}p$ (XIV.)

$(p\text{-}C_7H_7{\cdot}SO_2)_2NH$ (XV.) $Ph{\cdot}CO{\cdot}NH{\cdot}SO_2Ph$ (XVI.) $[CH_3{\cdot}CO{\cdot}N{\cdot}SO_2{\cdot}C_6H_4{\cdot}p]^-{}_2Co^{++},6H_2O$ (XVII.)

twelve metallic salts have been isolated as hydrates, ammines, or in the anhydrous condition from *N*-toluene-*p*-sulphonylacetamide (XIV), *NN*-ditoluene-*p*-sulphonylamine (XV), and *N*-benzoylbenzenesulphonamide (XVI). They prove to be water-soluble crystalline substances, sparingly or not at all soluble in organic solvents, with colours characteristic of the metallic ion they possess. On being heated, they decompose without true melting, although the highly hydrated salts appear to dissolve in their water of hydration. They are therefore judged to have structures in which the metal is electrovalently attached, as in cobaltous *N*-toluene-*p*-sulphonylacetamide hexahydrate (XVII), and structures such as (III) and (IV) (H = metal) for these derivatives are completely untenable. It is doubtless on this account that amides and diacylamines fail to give the ferric chloride colour test.

Experimental.

(The analytical data given below for water of hydration do not always conform to those required owing to the difficulty of dehydrating these acylated compounds without causing hydrolysis.)

*Metallic Salts of N-Toluene-*p*-sulphonylacetamide.*—These were prepared, unless otherwise stated, by the action of the appropriate carbonate on an aqueous alcoholic solution of the above. The *lithium* salt monohydrate formed white rectangular plates, readily soluble in water, alcohol, and acetone, insoluble in other organic solvents or in moist toluene (Found: N, 5·8; Li, 2·8; loss at 100°, 9·3. $C_9H_{10}O_3NSLi,H_2O$ requires N, 5·9; Li, 2·9; H_2O, 7·6%). The *sodium* salt monohydrate formed white crystals from water (Found: N, 5·5; Na, 8·9; loss at 100°, 7·9. $C_9H_{10}O_3NSNa,H_2O$ requires N, 5·5; Na, 9·1; H_2O, 7·1%). The *diamminocupric* salt was obtained as royal-blue crystals on mixing equivalent weights of copper sulphate and toluene-*p*-sulphonylacetamide in concentrated aqueous ammonia. It was insoluble in water and in organic solvents, and was stable in a vacuum-desiccator over sulphuric acid (Found: total N, 10·5; NH_3, 6·4. $C_{18}H_{30}O_6N_6S_2Cu,2NH_3$ requires total N, 10·7; NH_3, 6·5%). Attempts to prepare a copper derivative in the absence of ammonia yielded only basic compounds.

The *barium* salt monohydrate formed white needles, moderately soluble in water, insoluble in organic solvents (Found: N, 4·8; Ba, 23·7; loss at 100°, 3·1. $C_{18}H_{20}O_6N_2S_2Ba,H_2O$ requires N, 4·8; Ba, 23·7; H_2O, 3·1%). The *cobaltous* salt hexahydrate formed pink hexagonal plates from water (Found: N, 4·5; Co, 9·95; loss at 100°, 18·8. $C_{18}H_{20}O_6N_2S_2Co,6H_2O$ requires N, 4·7; Co, 10·0; H_2O, 18·3%), yielding a blue anhydrous salt which reverted to pink in water. The *nickel* salt nonahydrate formed green rhombs from water (Found: N, 4·4; Ni, 9·1; loss over H_2SO_4 (vac.), 20·4. $C_{18}H_{20}O_6N_2S_2Ni,9H_2O$ requires N, 4·3; Ni, 9·1; H_2O, 25·1%). The *manganous* salt nonahydrate was obtained by double decomposition of the sodium salt with manganese sulphate as cream-coloured rhombs from water (Found: N, 4·3; Mn, 8·5; loss at 100°, 25·2. $C_{18}H_{20}O_6N_2S_2Mn,9H_2O$ requires N, 4·4; Mn, 8·6; H_2O, 25·3%). A ferrous salt was obtained as pale green plates rapidly becoming brown, insoluble in organic solvents, and was not analysed.

*Metallic Salts of NN-Ditoluene-*p*-sulphonylamine.*—The amine, m. p. 174° (Found: N, 4·2. Calc.: N, 4·3%), was treated in aqueous alcoholic solution with the appropriate metallic carbonate. The *cupric* salt dodecahydrate formed pale blue needles from water (Found: Cu, 6·8; loss at 100°, 23·0. $C_{28}H_{32}O_4N_2S_4Cu,12H_2O$ requires Cu, 6·8; H_2O, 23·3%). The *barium* salt monohydrate formed white needles from water (Found: Ba, 16·9; loss at 100°, 2·3. $C_{28}H_{32}O_4N_2S_4Ba,H_2O$ requires Ba, 17·1; H_2O, 2·2%). The *nickel* salt 13-hydrate formed green rhombs from water (Found: N, 3·0; Ni, 6·2; loss over P_2O_5 (vac.), 19·2. $C_{28}H_{32}O_4N_2S_4Ni,13H_2O$ requires N, 3·0; Ni, 6·2; H_2O 24·8%); in addition to being readily soluble in water, it was sufficiently soluble to impart a green colour to alcohol, acetone, chloroform, and pyridine.

Metallic Salts of N-Benzoylbenzenesulphonamide.—This substance was sufficiently acid to decompose many metallic carbonates, but the resulting salts were seldom isolated in a pure condition owing to more or less extensive hydrolysis; *e.g.*, nickel and cobalt carbonates yielded green and pink solutions, respectively, but the resulting filtrates rapidly hydrolysed. The *potassium* salt formed white feathery crystals, very soluble in water (Found: K, 12·7. $C_{13}H_{10}O_3NSK$ requires K, 13·0%), and the *tetramminocupric* salt, prepared by mixing equivalent amounts of copper sulphate and *N*-benzoylbenzenesulphonamide in concentrated aqueous ammonia, formed royal-blue crystals (Found: total N, 12·4; Cu, 9·8; NH_3, 9·9. $C_{26}H_{30}O_6N_6S_2Cu,4NH_3$ requires total N, 12·9; Cu, 9·8; NH_3, 10·0%). It was hydrolysed by water, giving a blue solution and a white precipitate.

The following new compounds were prepared for molecular-weight measurements in the course of this work: *methyl* N-*acetyl*-N-*methylcarbamate*, b. p. 174—176° (Found: N, 10·4. $C_4H_9O_3N$ requires N, 10·7%), and *ethyl* N-*acetyl*-N-*ethylcarbamate*, b. p. 191—192° (Found: N, 8·65. $C_7H_{13}O_3N$ requires N, 8·8%), both colourless liquids of peppermint odour; N-*benzenesulphonylacet*-*p*-*anisidide*, white crystalline solid (from alcohol), m. p. 142° (Found: N, 4·5. $C_{15}H_{15}O_4NS$ requires N, 4·6%). *Methyl*

2-pyridylcarbamate formed white crystals (from alcohol), m.p. 130° (Found: N, 18·3. $C_{71}H_{104}O_4N_4$ requires N, 18·4%).

Molecular-weight Data.—Molecular weights were measured cryoscopically, the majority in nitrobenzene solution, but those recorded in italics in benzene solution. In the tables, concentrations are expressed as g.-mols. ($\times 10^3$)/100 g. of solution; *M* is the apparent molecular weight deduced according to ideal-solution laws; the association factor (a) is calculated as the ratio of *M* to the formula weight. The extremely steep curve for *NN*-ditoluene-*p*-sulphonylamine (Fig. 3) in nitrobenzene solution calls for comment. Although the values for a may have no absolute significance, that the substance is substantially associated is indicated by the flatness of the curve for this substance in dioxan solution (Fig. 3), indicating a complete loss of association in the latter solvent.

University College, Leicester. [*Received, May 4th*, 1950.]

---

555. *The* Euphorbia *Resins. Part V. Oxidative Degradation in the Side Chain of Euphol.*

By Hans K. Krüsi.

Euphyl acetate was dehydrogenated with *N*-bromosuccinimide and the resulting acetate mixture, containing a new euphatrienyl acetate (I), was oxidised with chromium trioxide. From the reaction mixture was isolated a degradation acid (III), $C_{33}H_{54}O_5$, which was purified by way of the methyl ester (II), $C_{34}H_{56}O_5$, of its acetyl derivative, and on esterification gave a methyl ester (IV), $C_{31}H_{52}O_5$.

Euphol, $C_{30}H_{50}O$, was characterised by Newbold and Spring (*J.*, 1944, 2497) as a tetracyclic triterpene alcohol containing one active and one inactive ethylenic linkage. The active double bond was shown by Jeger and Krüsi (*Helv. Chim. Acta*, 1947, **30**, 2045) to exist as an *iso*propylidene group which, according to McDonald, Warren, and Williams (*J.*, 1949, 155) was not attached directly to a ring but formed part of a longer chain. The present communication is concerned with the degradation of this carbon chain.

Euphyl acetate, $C_{32}H_{52}O_2$, was heated under reflux with 1 mole of *N*-bromosuccinimide in carbon tetrachloride with light as catalyst (Wohl–Ziegler). Purification of the product led to a mixture of acetates, m. p. 105—106°, which gave a brown colour in tetranitromethane and depressed the m. p. of euphyl acetate by 2°. The ultra-violet extinction curve of the acetate mixture showed the presence of three maxima: at $\lambda = 232$ mμ. (log $\varepsilon = 3{\cdot}50$), 238·5 mμ. (log $\varepsilon = 3{\cdot}52$), and 247 mμ. (log $\varepsilon = 3{\cdot}33$). The extinction curve is different from that of the starting material, but the values of λ at the three maxima are similar to those of dihydroagnosterol (and γ-lanosterol), which also contains a system of double bonds. Bellamy and Dorée (*J.*, 1941, 178) report maxima at $\lambda = 236$, 244, and 250 mμ., and Ruzicka, Denss, and Jeger (*Helv. Chim. Acta*, 1946, **29**, 206) report a maximum at 240 mμ. The low extinction values of the mixture indicated the presence of impurities in what was essentially the compound (I), containing a system of conjugated double bonds.

$C_{19}H_{29}$ {–CH_2·CH_2·CH:CMe_2; –CH_2·C(OH)·CH_2·; >CH·OH} (V.)

$C_{19}H_{29}$ {–CH:CH·CH:CMe_2; –CH_2·C(OAc)·CH_2·; >CH·OAc} (I.)

$C_{19}H_{29}$ {–CO_2R; –CO·C(OH)·CO·; >CH·OR′}
(II; R = Me, R′ = Ac.)
(III; R = H, R′ = H.)
(IV; R = Me, R′ = H.)

Oxidative degradation of the acetate mixture with chromium trioxide gave neutral and acidic reaction products in the ratio 1 : 2; both fractions were oily. Chromatographic separation of the neutral part gave no crystalline organic eluates. The acidic oils were esterified with diazomethane, giving in good yield the methyl ester $C_{34}H_{56}O_5$ (II) of a diketo-acetoxy-acid, readily hydrolysed to the corresponding diketo-hydroxy-acid (III), $C_{33}H_{54}O_5$. The ease of hydrolysis indicated the presence of a primary or secondary carboxyl group. The action of diazomethane on the acid (III) gave its methyl ester (IV), $C_{34}H_{54}O_5$.

The ultra-violet extinction curves of the acid (III) ($\lambda_{max.} = 272$ mμ., $\log \varepsilon_{max.} = 3{\cdot}99$) and of the ester (II) ($\lambda_{max.} = 271{\cdot}5$ mμ., $\log \varepsilon_{max.} = 3{\cdot}94$) were similar to those found by Haines and Warren (*J.*, 1950, 1562) for diketodihydroeuphyl acetate ($\lambda_{max.} = 275$ mμ., $\log \varepsilon_{max.} = 3{\cdot}94$), which was believed to contain the chromophoric system –CO–C=C–CO–.

The results of the molecular-weight determination of the diketo-hydroxy-acid (III) and of the methyl ester (II) exclude molecular formulæ containing either more or less oxygen.

The new C_{31}-diketo-hydroxy-acid (III) is therefore a tetracyclic degradation product of euphol (V) containing the original hydroxy-group of the starting material, the grouping ·CO·C:C·CO· as chromophoric system, and a primary or secondary carboxyl group. It was probably formed by introduction of a new double bond in conjugation with the isopropylidene group by dehydrogenation to give (I), followed by oxidative fission of five carbon atoms with simultaneous formation of the chromophoric system.

Further work on the separation of the dehydrogenation mixture, the structure of the degradation products, and application of the same methods to related triterpenes is in progress.

Experimental.

(Microanalyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorr.)

Dehydrogenation of Euphyl Acetate with N-Bromosuccinimide.—*N*-Bromosuccinimide (0·78 g., 1·03 mols.; purity 99·5%) was added to euphyl acetate (2 g.), m. p. 104—105°, in carbon tetrachloride (50 ml.), and the solution heated under reflux for 1 hour; hydrogen bromide was evolved and succinimide began to float on the surface of the solution. Pyridine (5 ml.) was then added to the reaction mixture, which was boiled for a further 15 minutes. The solution was cooled, succinimide filtered off, and the filtrate distilled under reduced pressure on a steam-bath. The brown, oily residue was reacetylated with acetic anhydride–pyridine (1 : 1; 5 ml.) and dissolved in ether. The ethereal solution was washed with dilute sulphuric acid, saturated potassium carbonate solution, and finally water. The brown residue (1·8 g.), obtained after evaporation of the solvent, was dissolved in light petroleum (b. p. 50—70°) and percolated through a column of alumina (15 g.; activity I—II). The same solvent (50 ml.) eluted a yellow oil (1·2 g.). The more strongly adsorbed material could not be obtained in crystalline form from the fractions eluted later. The first fraction (1·2 g.) was again washed with light petroleum through a column of alumina (40 g.): (i) 10 ml. (30 mg.), (ii) 10 ml. (800 mg.), (iii) 10 ml. (200 mg.), (iv) 20 ml. (50 mg.). The later fractions were neglected.

All four fractions were obtained as oils, but fractions (ii) and (iii) crystallised after the addition of a few drops of ethanol. A solution of the crystals in ethanol gave an amorphous solid on cooling. Seeding and shaking the ethanol solution, however, gave crystals. Four such recrystallisations gave the acetate mixture as long needles, m. p. 105—106°, which, mixed with euphyl acetate, m. p. 107°, gave a depression of 2°. In tetranitromethane the surface of the crystals was coloured dark brown, giving later a brown-yellow solution. For analysis the crystals were dried over phosphoric oxide at 70° in a high vacuum for 2 days (Found: C, 81·9; H, 10·7. Calc. for $C_{32}H_{52}O_2$: C, 82·3; H, 10·8. Calc. for $C_{33}H_{54}O_2$: C, 82·0; H, 11·2%).

Oxidation of the Acetate Mixture with Chromium Trioxide.—Chromium trioxide (800 mg.) in acetic acid (8 ml.) was added to the acetate mixture (440 mg.) in acetic acid (50 ml.) at 40°. The mixture was kept for 7 hours at 40—45°, and then overnight at room temperature. It was poured into water (500 ml.), treated with a solution of potassium iodide (2 g.) in *N*-sulphuric acid(20 ml.), and titrated against 0·1*N*-sodium thiosulphate (Found: equivs. of oxygen used, 17·9). The water-insoluble oxidation product was filtered off and dissolved in ether, and the ethereal solution extracted with 10% potassium carbonate solution, *N*-sodium hydroxide, and water. The carbonate solution readily extracted a red, water-soluble potassium salt. The sodium hydroxide extract contained only traces of acid material. The neutral fraction (150 mg.), obtained by evaporation of the ether, was a dark yellow oil. Reacetylation as above and chromatographic separation gave no crystalline material.

The alkaline solution of the potassium salt was acidified with dilute sulphuric acid, and the yellow amorphous acid extracted with ether. The ethereal solution, washed until neutral with water, gave a yellow oil (290 mg.) which did not crystallise. This was treated with diazomethane in ether, and the ethereal solution washed with dilute sulphuric acid, potassium carbonate solution, and water. The methyl ester remained in the ether and crystallised after removal of this solvent in thick, long needles, m. p. 160—162°. The crystals were dissolved in light petroleum and adsorbed on activated alumina (20 g.). The same solvent (260 ml.) eluted yellow needles (220 mg.) which, after recrystallising 4 times from alcohol, gave the *diketo-acetoxy-acid methyl* ester (II), m. p. 170—171°. The substance was sublimed in a high vacuum at 165° (block-temp.), and then had m. p. 168—170° [Found: C, 71·5; H, 8·3%: *M* (Rast), 469. $C_{33}H_{46}O_6$ requires C, 71·2; H, 8·5%; *M*, 472·6].

Hydroxy-diketo-acid (III).—The above ester (II) 160 mg.) was refluxed with 10% alcoholic potash (20 ml.) for 2 hours. The acidified reaction mixture was extracted with ether, which was re-extracted with 10% sodium carbonate solution. Neutral hydrolysis products were not isolated. The reddish alkaline solution of the water-soluble sodium salt was neutralised with dilute sulphuric acid to yield yellow needles (150 mg.). Four crystallisations from acetone–water gave the *hydroxy-diketo-acid* (III), m. p. 233—234°. A specimen sublimed at 195—200° in a high vacuum gave thick yellow prisms, m. p. 231—233°, and a brown oily residue [Found: C, 71·9; H, 8·8%; *M* (Rast), 425; equiv. (Pregl), 383. $C_{31}H_{44}O_5$ requires C, 72·1; H, 8·7%; *M*, 416·5].

Methyl ester (IV). The hydroxy-diketo-acid (III) (50 mg.) was added to diazomethane in ether. The ethereal solution was washed with *N*-sulphuric acid, 10% potassium carbonate solution, and water, and gave on evaporation, a crystalline solid which was purified by percolating through a column of alumina (2 g., activity I—II). Mixtures of light petroleum and benzene (10 : 1—1 : 1) eluted yellow needles, m. p. 172—177°. Recrystallisation of the combined fractions from chloroform–methanol, and sublimation at 160° in a high vacuum gave long, thin, yellow needles of the *methyl* ester (IV), m. p. 185—188° after sintering at 181° (Found: C, 72·6; H, 9·0. $C_{32}H_{46}O_5$ requires C, 72·5; H, 8·8%). On admixture with the methyl ester (II) the m. p. was indefinite between 135° and 145°.

The author gratefully thanks Professor F. L. Warren, of these laboratories, for much helpful discussion and for the correction of the manuscript, and Mr. E. C. Leisegang, also of these laboratories, for the determination of the extinction curves.

UNIVERSITY OF NATAL, PIETERMARITZBURG, S. AFRICA. [*Received, June 28th*, 1950.]

---

556. *The Isolation and Identification of* (−)-*Stachydrine Ethyl Ester Periodide from the Root of* Courbonia virgata.

By ALAN J. HENRY and HAROLD KING.

The aim of the investigation was to examine the periodides, other than that of tetramethylammonium iodide, precipitated by Wagner's reagent from toxic extracts of the root of *Courbonia virgata*. One such periodide has been isolated in the crystalline state and identified as (−)-stachydrine ethyl ester tri-iodide.

IN recent years several references have been made to the incidence of toxic properties amongst the members of the Capparidaceae. Folkers (*J. Amer. Pharm. Assoc.*, **1938**, **27**, 689) recorded the presence of a substance with curare-like properties in *Capparis sola*; van der Walt and Steyn (*Onderstepoort J. Vet. Science*, **1943**, **18**, 207) demonstrated the toxic properties of *Boscia foetida* Schinz. and *Cadaba juncea*; *Capparis tomentosa* has long had a reputation in the Sudan for being toxic to camels; and Henry (*Brit. J. Pharmacol.*, **1948**, **3**, 187) reported the presence in *Courbonia virgata* A. Brongn. of a salt of tetramethylammonium hydroxide (tetramine) in sufficient concentration to render the plant quite highly toxic, the toxic action being a typical curare-like effect in conformity with the known physiological properties of this base. *Courbonia pseudopetalosa* Gilg and Benedict, from Nigeria, has also been shown (Henry, unpublished results) to contain the tetramethylammonium base in about the same concentration as in *C. virgata*. The chemical constituents of *Courbonia virgata* were further investigated by Henry and Grindley (*J. Soc. Chem. Ind.*, **1949**, **68**, 9) who reported the presence in the plant of di- and tri-methylamine and the probable presence of other bases, apparently of a quaternary nature, in addition to tetramethylammonium hydroxide.

The method of isolation of tetramine from *C. virgata* employed by Henry (*loc. cit.*) and by Henry and Grindley (*loc. cit.*) consisted in the precipitation of the base as its periodide by addition of a substantial excess of Wagner's reagent (iodine in potassium iodide) to the previously purified ethanol extract of the plant material, decomposition of the periodide by heating it with water, evaporation to dryness, and washing of the residue with ethanol to remove readily soluble iodides and undecomposed periodides (see below), followed by recrystallisation from hot water. Tetramethylammonium periodide, when pure, melts above 100°, and its decomposition to the iodide by heating with water on the water-bath proceeds smoothly, as it is fairly soluble in hot water. The periodide precipitate produced from a purified extract of *C. virgata* plant material contains in addition to tetramethylammonium periodide the periodides of other basic constituents, of much lower melting points and not so readily decomposable by heating with water, together with, apparently, other constituents not removed by basic lead acetate treatment but precipitable by iodine–potassium iodide. It is the further investigation of these residual periodides, and the bases producible from them, which has led to the isolation, as its crystalline periodide, of a quaternary base which has been identified as (−)-stachydrine ethyl ester. It is unlikely that this ester is an artefact produced from the plant betaine, stachydrine, during the process of isolation. Ethyl esters have been detected in the plant kingdom but infrequently. Molasses are said to contain an ethyl ester which in view of the finding of stachydrine ethyl ester may possibly be betaine ethyl ester.

EXPERIMENTAL.

Isolation of (−)-*Stachydrine Ethyl Ester Periodide.*—Five kg. of root material of *C. virgata*, air-dried and ground to pass a 30-mesh sieve, were digested for 8 hours on the water-bath, in 1-kg. lots, with rectified spirit (2 l.); the rectified spirit, which was acid in reaction, was filtered off and the residue washed with ethanol, re-extracted in the same way, and filtered. The spirit used for the second extraction of each lot was used for the first extraction of the next lot. The bulk of the spirit was distilled, then the residue was evaporated to a thick liquid by heating on the water-bath for several hours. The residue was diluted to 2·5 l. with distilled water and freed completely from fatty material by a preliminary treatment with molten paraffin wax, followed by several extractions of the cold, filtered solution first with light petroleum and then with chloroform. The solution, still intensely coloured, was then made alkaline with ammonia solution and exhaustively extracted with chloroform, then with ether. These extracts after examination were discarded.

The extracted mother-liquor was treated with neutral lead acetate until the solution became acid, then with basic lead acetate, of which large quantities were required, until no further precipitation took place. The filtrate was then added to four times its volume of ethanol which caused further heavy precipitation, the filtrate from which was evaporated to about 350 c.c. to remove the ethanol and then freed from lead by hydrogen sulphide after extensive dilution. The filtrate, which was still intensely coloured, was evaporated to 350 c.c., ammonium iodide (75 g.) in water (100 c.c.) added to the hot solution, and the solution placed in the refrigerator overnight. This treatment removed the bulk of the tetramine as the iodide, the yield of which was 71 g. The mother-liquor was transferred to a 1-5-l. beaker and heated to 60°, a layer of light petroleum added to sink the periodide, then excess of iodine solution (850 c.c. of 2·5% iodine in 18% ammonium iodide) added slowly with stirring. The precipitated periodide, which collected as a fluid layer 1 cm. thick at the bottom of the beaker, was covered with a half-inch layer of chloroform, in which it has low solubility, and the supernatant aqueous layer syphoned off as completely as possible. The beaker was then filled with water, and the aqueous layer again syphoned off, this process being repeated several times to effect complete removal of the water-soluble impurities—ammonium iodide, glucose, and fructose (produced by inversion of the sucrose present in the root), potassium salts, acetic acid, etc.—which were present in large quantities. The periodide was collected as completely as possible by the aid of rectified spirit, which was then removed on the water-bath, to give a mobile layer of periodide 1 cm. deep in a 1-5-l. beaker. To make quite certain that all undesirable impurities were removed, the periodide layer was twice treated on the water-bath with water (1 l.), and the aqueous extract discarded. The decomposition of the periodides to the iodides of the bases was now proceeded with, by prolonged heating on the water-bath with much stirring and occasional decanting of the aqueous extract into evaporating dishes and evaporation to low bulk. It was at this stage that the main difficulties began to be encountered as, unlike the decomposition of tetramine periodide which proceeds smoothly, it was found that the iodine clung with great tenacity to the solution, owing to the stability of some of the periodides present.

As decomposition of the periodide proceeded, much of its mobility was lost until, by the time some 30—40% had been decomposed, the residue could be dried to a friable solid, part of which could be dissolved in ethanol leaving a very inactive solid residue which still contained a high proportion of available iodine. The solution containing the bulk of the iodides of the more readily decomposable periodides was treated with purified animal charcoal, filtered, and evaporated almost to dry dryness on the water-bath with much blowing with the fan over the surface, and the residue extracted with absolute ethanol to separate the bulk of the remaining tetramine iodide, which has low solubility in ethanol. When kept, the ethanol solution acquired an intensely dark colour; it was transferred to an evaporating basin and the ethanol evaporated. On treatment of the residue with water a nearly colourless aqueous solution resulted but a substantial globule of fluid periodide (X) was present. After some days, large crystals of a periodide slowly formed in the filtered aqueous solution, which by then had become quite brown. Crystallisation was therefore allowed to proceed for 16 days, by which time a substantial crop had formed. The crystals were collected, washed with ice-cold distilled water and dried (yield G_1 = 1·09 g.). The crystals had only a very slight odour of iodine. The mother-liquor from this crop of crystals was set aside at room temperature, whereupon more crystals, apparently identical with the first crop, soon began to form. After 20 days the crystals were collected as before (yield G_1' = 1·53 g.). Subsequent analysis showed the two crops to be identical. The filtrate from this crop, when kept, produced further crystals of similar appearance to the first two crops, but these proved to be heavily contaminated with a fluid periodide; whilst the fourth crop of periodide which the solution yielded was essentially fluid.

The fluid periodide (X) was dissolved in hot ethanol (*ca.* 100 c.c.) and allowed to cool, substantial crystallisation occurring. The crystals were collected, washed with cold ethanol, and dried to constant weight (yield G_2 = 3·73 g.). The filtrate, after a preliminary concentration, was kept at room temperature until the ethanol had evaporated completely. The periodide residue was at first fluid, but on further storage much crystallisation had occurred. On treatment of the residue with ethanol (5 c.c.) much dissolved, but a substantial crystalline residue remained, which was filtered off, washed with ice-cold ethanol (30 c.c.), then with much ice-cold water, and dried to constant weight (yield G_2' = 1·86 g.). These two crops were shown to be identical with G_1 and G_1'. The total weight of the specimens G (8·2 g.) represents only a small fraction of the original periodide precipitated from the extract of the 5 kg. of root material. At least one other periodide, fluid at the ordinary temperature and readily soluble in ethyl and amyl alcohols, is present and will be further investigated as opportunity occurs.

Identification of the Crystalline Periodide as (−)-Stachydrine Ethyl Ester Tri-iodide.—Both specimens of *periodide* G_1 and G_1' crystallised in stout prisms (Found, in G_1: C, 19·6, 19·4; H, 3·5, 3·2; N, 2·7, 2·9; I, 71·4. In G_1': C, 19·8, 19·4; H, 3·3, 3·5; N, 2·7; I, 72·2, 71·9. $C_9H_{19}O_2NI_3$ requires C, 19·5; H, 3·6; N, 2·5; I, 68·6%). The high iodine values, in view of the excellent values for carbon, hydrogen, and nitrogen, are possibly due to salts occluded in the microanalytical method employed.

(−)-Stachydrine ethyl ester picrate. The periodide (0·5 g.) was dissolved in 50% ethanol and treated with excess of silver powder. The colourless solution was concentrated to a very small volume (1 c.c.) and treated with excess of saturated aqueous sodium picrate. The *picrate* (0·14 g.) crystallised readily, m. p. 101° (Found: C, 45·9, 44·5, 44·8; H, 4·9, 5·5, 5·0; N, 13·7, 13·9; EtO, 14·3, 20·8, 25·4. $C_9H_{19}O_2N,C_6H_3O_7N_3$ requires C, 45·0; H, 5·0; N, 14·0; EtO, 11·3%). The ethoxy-values were obtained by two independent micro-analysts; the high values are attributed to mobilisation of the *N*-methyl groups, possibly through intermediate methyl ester formation. For (±)-stachydrine ethyl ester picrate Schultze and Trier (*Z. Physiol. Chem.*, 1910, **67**, 87) give m. p. 94—96°.

Optical rotation. An approximate value for this constant was obtained by treating the periodide (1·035 g.) with silver powder in aqueous ethanol, filtering, removing the alcohol, and diluting the residue to 25 c.c. with water; $[\alpha]_D^{20}$ −4·4°, calculated as iodide.

(−)-*Stachydrine Ethyl Ester Aurichloride and Platinichloride.*—The aqueous iodide solution from the optical-rotation determination was treated with excess of freshly precipitated silver chloride, filtered, and evaporated to dryness. The residual striated mass of crystals was dissolved in water (1 c.c.), and a portion (0·5 c.c.) treated with gold chloride solution. The precipitated oily ***aurichloride*** rapidly crystallised in small needles (0·3 g.), m. p. 61—62°. Schultze and Trier (*loc. cit.*) give m. p. 59—60° for the (±)-salt (Found: C, 21·3; H, 3·5; Au, 38·7. $C_9H_{14}O_3NCl_4Au$ requires C, 21·1; H, 3·5; Au, 38·6%). The remainder of the parent solution of chloride (0·5 c.c.) was treated with chloroplatinic acid solution and gave a platinum salt as clusters of tiny needles, m. p. 195° (decomp.).

Attempted Synthesis of (−)-*Stachydrine Ethyl Ester.*—L-Proline, $[\alpha]_D^{20}$ −85·5° (1·3 g.), was methylated in methanol solution with sodium hydroxide and excess of methyl iodide (King, *J.*, 1941, 338). The neutral solution was diluted with water, excess of silver chloride was added, and after filtration the solution was evaporated to dryness and the methylated product dissolved in absolute ethanol to remove sodium chloride. At this stage the solution was checked for optical activity and had $[\alpha]_D^{20}$ −24° (calculated on the assumption that the product was stachydrine hydrochloride). Yoshimura and Trier (*Z. physiol. chem.*, 1912, **77**, 292) give $[\alpha]_D^{20}$ −26° for this salt. The ethanolic solution was then treated with 1 pellet of sodium hydroxide and boiled to hydrolyse any methyl ester formed during the methylation process. Aqueous hydrochloric acid was added until the solution was slightly acid, and the solution was then evaporated to dryness and the residue extracted with absolute ethanol to remove sodium chloride. The ethanolic solution was saturated with hydrogen chloride at −5° and then boiled for 3·5 hours. The solution was finally evaporated to dryness under reduced pressure, and the residue dissolved in water (5 c.c.). This solution was now optically inactive. The picrate, aurichloride, and platinichloride were readily obtained in crystalline form and must be regarded as the salts of (±)-stachydrine ethyl ester. A comparison of their m. p.s and mixed m. p. behaviour with the corresponding salts of (−)-stachydrine ethyl ester is shown below.

	(−)-Stachydrine ethyl ester.	Mixture.	(±)-Stachydrine ethyl ester.
Picrate	101—102°	102—103°	103—104°
Gold salt	63—64	59—60	58—60
Platinum salt	195 (decomp.)	195—198	196—198

These salts are extremely difficult to recrystallize without change; a small portion of both picrates on recrystallisation separated from water in prisms, both showing m. p. 104—105°. It seems possible that the m. p. of these three salts are the same for the (−)- and (±)-esters.

From the above it is clear that racemization has occurred, probably at the stage when the methanolic solution of (−)-stachydrine or its methyl ester was boiled with alkali. To avoid this, the experiment was repeated but with omission of the alkaline treatment. The ethanolic solution of the neutral methylation product of L-proline was saturated with hydrogen chloride as described above, and an aqueous solution of the ester hydrochloride obtained in the same way. The picrate and gold and platinum salts were obtained crystalline, and a comparison of their m. p.s with those of the natural product from *Courbonia virgata* is shown below.

	(−)-Stachydrine ethyl ester.	Mixture.	Synthetic product from L-proline.
Picrate	101—102°	96—97°	96—97°
Gold salt	63—64	65—68	70—73
Platinum salt	195 (decomp.)	199 (decomp.)	204

The lack of agreement shown in this table is pronounced, and the conclusion is drawn that the synthetic product prepared in this way must contain some methyl ester from the original methylation process. In this connection, the m. p. 70—73° observed above for the gold salt may be significant since Jahns (*Ber.*, 1896, **29**, 2067) gives m. p. 85° for (±)-stachydrine methyl ester aurichloride.

WELLCOME CHEMICAL LABORATORIES, MINISTRY OF HEALTH, KHARTOUM.
NATIONAL INSTITUTE FOR MEDICAL RESEARCH,
MILL HILL, N.W.7.

[*Received, July 8th*, 1950.]

---

557. *The Constituents of the Wood of* Castanospermum australe *Cunn. et Fras. Part I. The Isolation of a New Sapogenin, Castanogenin.*

By J. J. H. SIMES.

Extraction of the wood of *Castanospermum australe* gives a crude saponin which on hydrolysis yields a mixture of sapogenins, one of which, castanogenin, has been characterized as a new sapogenin having the formula $C_{30}H_{48}(OH)_3(CO_2H)_3$.

In an investigation of some Australian woods for saponin content, it was noted that *Castanospermum australe* gave strongly positive tests, and the present work was undertaken to investigate the saponin present in the wood. This large tree, more commonly known as "Black Bean" and sometimes called the "Moreton Bay Chestnut," occurs in the brush forests of northern New South Wales and Queensland. The seeds of the tree are reported to be

poisonous to stock, although on analysis no poisonous principle was detected (see Hurst, "The Poison Plants of New South Wales," Sydney, 1942, p. 153).

Extraction of the wood (see Experimental section for details) gave fats, phenols, sugars, and sapogenins. It was difficult to obtain crystalline material from the crude sapogenin; the method eventually adopted was to carry out a fractionation by long extraction with ether, whereafter the ether-soluble portion could be crystallized from methanol. This was resolved by fractional crystallization from methanol into a more soluble sapogenin, castanogenin, and a less soluble one not yet investigated.

Analyses of castanogenin and its derivatives are consistent with the molecular formula $C_{30}H_{44}O_6$ for castanogenin, and indicate the presence of two carboxyl and two hydroxyl groups. Attempts to reduce castanogenin, its diacetate, and its dimethyl ester with hydrogen using Adams's catalyst at room temperature were unsuccessful. With tetranitromethane castanogenin itself gives no colour; its more soluble derivatives, the diacetate and dimethyl ester, however, give deep yellow colours, indicating the presence of a carbon–carbon double bond which is evidently of the unreactive type present in triterpenes. The results of the investigation so far carried out agree with the classification of castanogenin as a new member of the triterpenoid acid class of sapogenins.

Experimental.

(M. p.s are uncorr.)

Isolation of the Saponin.—The dried wood (25 kg.) of *Castanospermum australe* was reduced to a fine saw-dust and steeped in ethanol. The red-brown alcoholic extract was drained off after 24 hours and replaced with fresh ethanol; this process was repeated 7 times, the wood being then practically exhausted. The combined alcoholic extracts were evaporated, finally in an open dish on a steam-bath, until most of the solvent had been removed leaving a black viscous mass. Addition of ether yielded a precipitate which was triturated with fresh portions of ether until it became a friable solid. Evaporation of the solvent from the ethereal extract left an intractable black material on the surface of which accumulated a small amount of a yellow fatty substance. The black material gave a red-brown colour in the Liebermann–Burchard test, and a green colour with neutral ferric chloride solution; the fatty substance gave no colour in either test. The crude saponin precipitated by ether became moist on exposure to the atmosphere and difficult to handle; it was thoroughly dried at 105° and then was no longer hygroscopic; the yield was 700 g. The crude saponin was readily soluble in water and ethanol, leaving a small residue in each case, and its aqueous solution on agitation gave a very large froth stable for up to 2 days. It gave a deep red colour, changing to purple, in the Liebermann–Burchard test. At a dilution of 1 in 20,000 in 0·9% saline solution it required 5 minutes to haemolyse completely a 1% suspension of sheep-blood corpuscles at 28°.

Hydrolysis of the Saponin.—A solution of crude saponin (80 g.) in hot water (1·5 l.) was freed from a small amount of insoluble matter by filtration with kieselguhr. It was then heated to boiling and sufficient 10*N*-hydrochloric acid added to make the solution approx. *N*. with respect to hydrochloric acid; a gelatinous precipitate immediately commenced to form and the mixture was boiled under reflux for 30 minutes, with vigorous stirring in the latter stages to overcome the frothing caused by the heavy gelatinous precipitate; the mixture was filtered hot. A sample of the filtrate was boiled for 4 hours with stronger acid and gave only a small amount of further precipitate, indicating that hydrolysis was virtually complete. The filtrate gave a strong test for reducing sugars with Fehling's solution; when left in the refrigerator for 2 days it deposited pale yellow needles of a substance which gave a green colour with neutral ferric chloride solution. The precipitate of sapogenins was extracted with boiling water until the extract no longer gave the ferric chloride colour (this process also removed the last traces of hydrochloric acid); this was found essential, as residual hydrochloric acid in the sapogenin caused considerable darkening on drying). The sapogenin was air-dried at 105°; yield (from 80 g. of saponin), 22 g. The crude sapogenin was a dark brown amorphous powder, insoluble in water, and soluble in ethanol and in aqueous and alcoholic sodium hydroxide solutions. It gave a deep red colour, changing to purple in the Liebermann–Burchard test.

Separation of the Sapogenins.—The crude sapogenin was easily soluble in many organic solvents but no crystalline material could be obtained from these solutions. Sublimation at 200—300/10^{-4} mm. produced some amorphous sublimate, containing a little crystalline material, with much decomposition. Attempts to purify the crude sapogenin through the sodium and potassium salts were also unsuccessful. Though the crude sapogenin was very sparingly soluble in ether, very extended extraction with ether in a Soxhlet apparatus removed a fraction which separated spontaneously from the ethereal extract and was much lighter in colour. 75 G. of material was extracted from 300 g. of crude sapogenin in 200 hours and even at this stage some sapogenin was still extractable; during the extraction 55 g. of light-brown amorphous solid (fraction *A*) separated spontaneously from the boiling ether, leaving 20 g. dissolved in the ethereal extract. Fraction *A* was boiled under reflux for 1 hour with methanol (300 ml.) and filtered hot, leaving a colourless residue consisting principally of the less soluble sapogenin. The methanolic solution was concentrated, causing crystallization to occur. In all 15 g. of crystals were obtained from this solution, which on further evaporation set to a gel. These were crystallized again from methanol and then from dioxan (which was the most satisfactory solvent for recrystallization) to the constant m. p. 380—382° (decomp.). An additional amount of this sapogenin, castanogenin, was also obtained by refrigeration of the ethereal solution remaining after filtering off fraction *A*. The total yield from 300 g. of crude sapogenin was 9 g.

Castanogenin.*—*Castanogenin was moderately soluble in methanol, ethanol, or dioxan, slightly soluble in ether, and practically insoluble in chloroform, light petroleum, or benzene. It crystallized as prisms from methanol and as needles from ethanol, dioxan, or ether, both forms having the same m. p. It gave a deep red colour, changing to purple, in the Liebermann–Burchard test and had $[\alpha]_D^{20}$ +107° (*c*, 1·06 in absolute ethanol) [Found: C, 71·7; H, 9·1; active H, 0·75%; equiv., 256. $C_{18}H_{42}(OH)_5(CO_2H)_2$ requires C, 71·7; H, 9·2; active H, 0·8%; equiv., 251] [the equiv. was determined by titration of an ethanolic solution with 0·1*N*-sodium hydroxide (phenolphthalein)].

Ethanolic sodium hydroxide solution was added to an ethanolic solution of castanogenin, giving a gelatinous precipitate of the ***disodium*** salt, very soluble in water, and slightly soluble in ethanol from which it crystallized in fine needles (Found: Na, 8·5. $C_{30}H_{44}O_9Na_2$ requires Na, 8·4%).

Diacetate. Castanogenin (2·5 g.), acetic anhydride (30 ml.), and anhydrous sodium acetate (2 g.) were boiled under reflux for 2 hours and then poured into water, yielding a white solid which recrystallized from methanol in colourless plates, which softened at 220°, formed a clear glass at 226°, and flowed at 239—240°, and had $[\alpha]_D^{20}$ +75° ±2° (*c*, 0·166 in chloroform; *l* = 4 dm.) and gave a yellow solution with tetranitromethane in chloroform [Found: C, 70·0; H, 8·5%; sap. val., 374; *M* (camphor), 561. $C_{36}H_{56}O_8$ requires C, 69·6; H, 8·6%; sap. val., 382; *M*, 586].

Dimethyl esters. Castogenin and diazomethane in ether gave the ***dimethyl*** ester as a crystalline material, soluble in methanol, ethanol, dioxan, or ether, recrystallizing from aqueous methanol in plates, m. p. 224—225°, $[\alpha]_D^{20}$ +80° ±4° (*c*, 0·084 in chloroform), and giving a yellow colour with tetranitromethane in chloroform [Found: C, 72·2; H, 9·5%; *M* (camphor), 518. $C_{32}H_{56}O_8$ requires C, 72·4; H, 9·5%; *M*, 530].

Castanogenin diacetate gave, as above, the ***diacetate dimethyl*** ester which crystallized from methanol in plates, m. p. 238·5—239°, $[\alpha]_D^{20}$ +90° ±3° (*c*, 0·127 in chloroform) (Found: C, 70·0; H, 9·1. $C_{36}H_{54}O_8$ requires C, 70·3; H, 8·9%).

The carbon, hydrogen, and active hydrogen analyses of castangogenin were carried out by Drs. Weiler and Strauss, Oxford. The author thanks Mr. E. R. Cole, Sydney Technical College, for the remaining carbon, hydrogen, and sodium analyses. The author also thanks Mr. L. Bryant, N.S.W. Forestry Commission, for supplying the ground wood of *Castanospermum australe*.

SYDNEY TECHNICAL COLLEGE, N.S.W., AUSTRALIA. [*Received, July 10th*, 1950.]

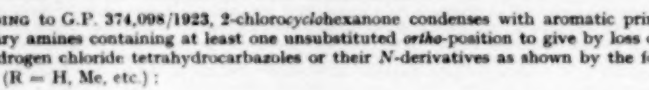
---

558. *The Preparation of Tetrahydrocarbazoles from 2-Chlorocyclohexanone.*

By NEIL CAMPBELL and E. B. MCCALL.

Methyl, dimethyl, chloro-, and carbomethoxy-derivatives of 1 : 2 : 3 : 4-tetrahydrocarbazole are readily prepared by condensation of 2-chlorocyclohexanone with excess of the appropriate aniline. The resulting tetrahydrocarbazoles and particularly the dimethyl derivatives readily form peroxides. The reaction of the 2-anilinocyclohexanones, intermediates in the above synthesis, with 2 : 4-dinitrophenylhydrazine has been studied.

ACCORDING to G.P. 374,098/1923, 2-chlorocyclohexanone condenses with aromatic primary or secondary amines containing at least one unsubstituted *ortho*-position to give by loss of water and hydrogen chloride tetrahydrocarbazoles or their *N*-derivatives as shown by the following scheme (R = H, Me, etc.):



(I.) (II.)

We have applied the method to eleven primary aromatic amines and with two exceptions have obtained the expected substituted 1 : 2 : 3 : 4-tetrahydrocarbazoles (II), generally in yields of 30—60%. Although these are only moderate, a one-stage process from easily accessible and cheap substances makes the method attractive not only for the preparation of tetrahydrocarbazoles but also for that of the corresponding carbazoles (cf. Barclay and Campbell, *J.*, 1945, 530). It is thus a useful supplement to the Graebe–Ullmann and Borsche methods, both of which have their limitations. We were never able to obtain the excellent or quantitative yields claimed in the patent, and it is somewhat difficult to accept the claims of the German workers since 2-chlorocyclohexanone with aniline yields *cyclo*hex-2-en-1-one (Kötz and Grethe, *J. pr. Chem.*, 1909, **80**, 491). The failures were with *o*- and *p*-bromoaniline and these are paralleled

by the failure of Verkade and Janetzky (*Rec. Trav. chim.*, 1946, **65**, 691) to prepare 5-bromo-2 : 3-dimethylindole by ring-closure of 2-*p*-bromoanilinobutanone.

2-Bromocyclohexanone was found to be less effective than 2-chlorocyclohexanone.

The method was successfully applied to the preparation of dimethyltetrahydrocarbazoles with both substituents in the aromatic ring. These substances have not so far been prepared, presumably because of the instability of the (dimethylphenyl)hydrazines (Klauber, *Monatsh.*, 1890, **11**, 285; Willgerodt, *J. pr. Chem.*, 1905, **71**, 399). An interesting property of the resulting dimethyltetrahydrocarbazoles was their readiness to absorb a molecule of oxygen during crystallisation from light petroleum, the main products being the less soluble oxygenated products which are probably peroxides as recently suggested by Beer, McGrath, Robertson, and Woodier (*Nature*, 1949, **164**, 362; cf. Witkop, *J. Amer. Chem. Soc.*, 1950, **72**, 1428). To minimise peroxide formation rapid crystallisation from the hot solutions is essential. The peroxides are characterised by their strong bluish-green fluorescence, especially in dilute methanolic solution.

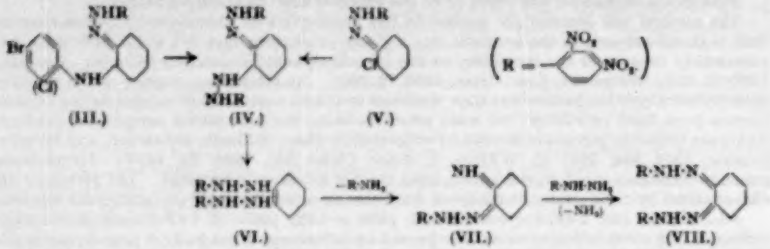
o-4-Xylidine and 2-chlorocyclohexanone gave a 13% yield of 6 : 7-dimethyltetrahydrocarbazole, the constitution of which was proved by dehydrogenation to 2 : 3-dimethylcarbazole identical with a sample prepared from 1-keto-6 : 7-dimethyl-1 : 2 : 3 : 4-tetrahydrocarbazole by Clemmensen reduction followed by chloranil dehydrogenation (Anderson and Campbell, *J.*, 1950, 2855). No trace of the 5 : 6-dimethyltetrahydrocarbazole was detected, and this is in agreement with Verkade and Janetzky's finding (*loc. cit.*) that *m*-toluidine and methyl α-bromoethyl ketone yield only one trimethylindole and not the two theoretically possible. Ring-closure appears to take place preferentially at a position *para* to a methyl group, and a similar result was found with *m*-chloroaniline, which with 2-chlorocyclohexanone gave only 7-chlorotetrahydrocarbazole. This substance was obtained as crystals, m. p. 171°, b. p. 250—260°/49 mm. No lower-boiling fraction indicative of the 5-isomer, which is a syrup at room temperature, was obtained. It is noteworthy that cyclisation of phenacyl-*m*-chloroaniline hydrochloride gives only one product (Bischler, *Ber.*, 1892, **25**, 2860) although in another type of cyclisation cyclohexanone *m*-chlorophenylhydrazone gives both 5- and 7-chlorotetrahydrocarbazole (Plant and Moggridge, *J.*, 1937, 1125). *m*-Aminobenzoic acid also gave tetrahydrocarbazole-7-carboxylic, but the yield (2·5%) makes comparisons unprofitable.

Aniline and 2-chloro-5-methylcyclohexanone gave a mixture of methyltetrahydrocarbazoles melting over a range of 3° and forming a maroon-coloured picrate with a wide m. p. range. Chloranil dehydrogenation afforded impure 2-methylcarbazole in 27% yield. These facts indicate that the product is 2- and possibly 3-methyltetrahydrocarbazole, the former resulting by the Bischler process or rearrangement (cf. Stevens and Cowper, *J.*, 1947, 1041; Brown and Mann, *J.*, 1947, 847, 858).

There can be little doubt from previous work on analogous syntheses that the above preparation of tetrahydrocarbazoles proceeds *via* intermediate 2-anilinocyclohexanones (I) (Bischler, *loc. cit.*; Strain, *J. Amer. Chem. Soc.*, 1929, **51**, 270; Julian *et al.*, *ibid.*, 1945, **67**, 1203; Cowper and Stevens, *loc. cit.*). These substances are readily prepared by heating the reactants in boiling ethanol with sodium carbonate or acetate. The yields are usually below 50%, again probably owing to dehydrohalogenation of the 2-chlorocyclohexanone. Cyclisation of the aminoketones was effected by heating them with aromatic amine hydrochlorides; but attempts with glacial acetic acid saturated with hydrogen bromide or acetic anhydride were unsuccessful. This supports Bischler's postulate of an intermediate anilino-anil (*loc. cit.*). It should be noted, however, that 4-aminoveratrole and 2-chlorocyclohexanone in the presence of sodium acetate gave 6 : 7-dimethoxytetrahydrocarbazole in 40% yield (Hughes and Lions, *J. Proc. Roy. Soc. N.S.W.*, 1937—38, **71**, 433). According to Bischler's theory it is the first arylamine molecule to react with the chloro-ketone which is eliminated in the cyclisation, and this is supported by the conversion of 2-*p*-bromoanilinocyclohexanone into tetrahydrocarbazole when heated with aniline hydrochloride.

When an attempt was made to prepare the 2 : 4-dinitrophenylhydrazone (as III) of 2-*p*-bromo- or 2-*o*-chloro-anilinocyclohexanones by Brady's method (*J.*, 1931, 756) the same halogen-free product, m. p. 233—234°, was obtained. This suggested that the hydrazine had not only condensed with the carbonyl group but had also displaced the halogenoanilino-residue to give the hydrazono-hydrazine (IV). The essential correctness of this assumption was confirmed by analysis of the products and by a study of the properties of 2-chlorocyclohexanone 2 : 4-dinitrophenylhydrazone (V) which, when heated with 2 : 4-dinitrophenylhydrazine or boiled in aqueous acetic acid, yielded the product of m. p. 233—234°. Presumably in the second case the dinitrophenylhydrazone undergoes partial hydrolysis, the "freed" dinitrophenylhydrazine then displacing the chlorine atom. Further examination of the product, m. p. 233—234°, showed,

however, that it is not (IV) but *cyclo*hexane-1 : 2-dione bis-2 : 4-dinitrophenylhydrazone (VIII) identical with a specimen prepared from the dione. This result (see also Bodforss



Ber., 1939, **72**, 468; von Auwers, *Ber.*, 1917, **50**, 1178) may be adequately explained in terms of Weygand's theory of osazone formation (*Ber.*, 1940, **73**, 1259; see also E. G. V. Percival, *Adv. Carbohydrate Chem.*, 1948, **3**, 43) in which intermediate dihydrazino-compounds and imino-derivatives, such as (VI) and (VII), respectively, are postulated.

Experimental.

Analyses were done by Drs. Weiler and Strauss, Oxford. By mixed m. p. is meant the m. p. of a substance when mixed with an authentic sample of proved constitution.

Preparation of Chloro-1 : 2 : 3 : 4-tetrahydrocarbazoles.—2-Chlorocyclohexanone was prepared by the methods of Meyer (*Helv. Chim. Acta*, 1933, **16**, 1291), Kotz and Grethe (*loc. cit.*), or preferably in 55% yield by the method given in *Org. Synth.*, **25**, 22, and can be stored in the refrigerator for long periods without decomposition. 2-Bromocyclohexanone is much less stable. 2-Chlorocyclohexanone (4 g.) was added slowly to *p*-chloroaniline (8 g.) at 150—160°, and the cooled mixture extracted with boiling ether. *p*-Chloroaniline hydrochloride (4·2 g., 85%) separated, and the filtrate was washed twice with dilute hydrochloric acid, and then with water. The dried (Na_2SO_4) ethereal solution gave 6-chloro-1 : 2 : 3 : 4-tetrahydrocarbazole (1·3 g., 20%), prisms (from methanol or light petroleum), m. p. and mixed m. p. 141—143°.

o-Chloroaniline (15 g.) and 2-chlorocyclohexanone (5 g.) similarly gave a brown syrup (2·2 g.), b. p. 180—200°/12 mm., which appeared to be chiefly 8-chloro-1 : 2 : 3 : 4-tetrahydrocarbazole. It formed a *picrate*, brick-red needles (from benzene), m. p. 138—140° (Found : N, 12·3. $C_{18}H_{11}O_7N_4Cl$ requires N, 12·9%). Dehydrogenation with chloranil gave 1-chlorocarbazole, prisms (from aqueous methanol), m. p. 113—115° (lit., 110° and 125°) (Found : Cl, 17·4. Calc. for $C_{12}H_8NCl$: Cl, 17·6%). The carbazole formed a picrate, dark orange needles (from benzene), m. p. 138—141°, and gave a bluish-green colour with a mixture of sulphuric and nitric acids. Impure 8-chloro-1 : 2 : 3 : 4-tetrahydrocarbazole was dissolved in xylene and after some days the crystalline *peroxide* separated, m. p. 134° (decomp.) (Found : C, 61·3; H, 5·3; N, 6·0; Cl, 14·8. $C_{12}H_{11}O_2NCl$ requires C, 60·6; H, 5·1; N, 5·9; Cl, 14·9%).

m-Chloroaniline (10 g.) and 2-chlorocyclohexanone (5 g.) at the b. p. of the former gave 7-chlorotetrahydrocarbazole, m. p. and mixed m. p. 179—180° (lit., 181°) (27%). It forms a *picrate*, maroon needles (from benzene), m. p. 128—130° (Found : N, 12·5%).

Preparation of Dimethylcarbazoles.—2-Chlorocyclohexanone (5 g.), *m*-4-xylidine (10 g.), and ethanol (20 ml.) were boiled for 16 hours, the ethanol evaporated, ether added, and the mixture filtered. The filtrate was washed successively with dilute hydrochloric acid, water, and sodium carbonate, and on evaporation gave 6 : 8-*dimethyltetrahydrocarbazole*, purified by distillation *in vacuo* followed by crystallisation from light petroleum; it had b. p. 235—240°/25 mm., and formed colourless prisms, m. p. 101—105° (Found : C, 84·9; H, 8·7; N, 7·0. $C_{14}H_{17}N$ requires C, 84·3; H, 8·6; N, 7·0%). It forms a *picrate*, chocolate-coloured needles (from benzene), m. p. 160—162° (Found : N, 12·6. $C_{20}H_{20}O_7N_4$ requires N, 13·1%). The tetrahydrocarbazole on recrystallisation from light petroleum gave immediately 50% of the purified tetrahydrocarbazole, and the mother-liquor gradually deposited the *peroxide*, colourless crystals, m. p. 116° (decomp.) (the m. p. depends on the rate of heating), sparingly soluble in benzene or light petroleum, but readily soluble in ethanol to give a strong green fluorescence (Found : C, 73·7; H, 7·7; N, 5·9%; *M*, 242. $C_{14}H_{17}O_2N$ requires C, 72·7; H, 7·4; N, 6·1%; *M*, 231). The peroxide does not form a picrate.

p-2-Xylidine similarly gave a 37% yield of 5 : 8-*dimethyltetrahydrocarbazole*, b. p. 215—220°/20 mm., m. p. 83—86°, needles (from light petroleum) (Found : C, 84·3; H, 8·4; N, 7·35%). The *picrate* separated as chocolate-coloured needles (from benzene), m. p. 138—141° (Found : N, 13·1%). The *peroxide*, prepared as for its isomer, formed yellow cubic prisms, m. p. 140° (decomp.) (Found : C, 72·7; H, 7·46; N, 6·1%).

o-4-Xylidine similarly yielded 6 : 7-*dimethyltetrahydrocarbazole*, elongated prisms, m. p. about 109° (13%), on rapid crystallisation from light petroleum (Found : C, 84·1; H, 8·6; N, 7·0%). It forms a *picrate*, chocolate-coloured needles (from benzene), m. p. 166—168° (Found : N, 13·0%). Crystallisation from light petroleum gave chiefly a product, m. p. 127° (decomp.), probably the peroxide, and this accounted for the above poor yield of the tetrahydrocarbazole. Dehydrogenation of the tetrahydro-

carbazole (0·6 g.) with chloranil (1·48 g.) in boiling sulphur-free xylene (15 ml.) for 24 hours, and passage of the product through a column of alumina ($2'' \times \frac{1}{2}''$), gave 2 : 3-*dimethylcarbazole*, colourless plates, m. p. 251—253° (42%) (Found : C, 86·2; H, 6·9. $C_{14}H_{13}N$ requires C, 86·2; H, 6·7%). It forms a *picrate*, scarlet needless (from benzene), m. p. 167—169° (Found : N, 12·6. $C_{20}H_{16}O_7N_4$ requires N, 13·1%). The carbazole does not give the characteristic bluish-green colour with concentrated sulphuric acid.

1 : 2 : 3 : 4-*Tetrahydrocarbazole-carboxylic Acids.*—2-Chlorocyclohexanone (5 g.) was added dropwise to methyl anthranilate (12 g.) at 140°, and the temperature was gradually raised to 160° during the addition. The mixture was kept at 160° for 15 minutes, cooled, boiled with dilute hydrochloric acid (50 ml.), and the residue extracted with boiling ether. The extract was washed with acid, and with sodium hydrogen carbonate solution, and the crude product obtained on evaporation was triturated with and recrystallised from methanol. Methyl 1 : 2 : 3 : 4-tetrahydrocarbazole-8-carboxylate was thus obtained in plates, m. p. 123—124° (lit., 124°) (crude yield, 34%) (Found : N, 6·1. Calc. for $C_{14}H_{15}O_2N$: N, 5·9%). It formed a *picrate*, brick-red needles (from benzene), m. p. 130—132° (Found : N, 11·6. $C_{20}H_{18}O_9N_4$ requires N, 12·2%), and was hydrolysed quantitatively by sodium hydroxide and ethanol to the acid, m. p. and mixed m. p. 200—201° (lit., 203°), also obtained in 35% yield by heating *o*-aminobenzoic acid and 2-chlorocyclohexanone at 150°.

Methyl 1 : 2 : 3 : 4-tetrahydrocarbazole-6-carboxylate was similarly prepared from methyl *p*-aminobenzoate (prepared in 80% yield by catalytic hydrogenation of methyl *p*-nitrobenzoate; *Org. Synth.*, **8**, 66), as leaflets (from aqueous acetic acid), m. p. 155—157° (lit., 158°) (30%). Hydrolysis gave 1 : 2 : 3 : 4-tetrahydrocarbazole-6-carboxylic acid, leaflets (from glacial acetic acid), m. p. and mixed m. p. 279—281° (lit., 282°). Attempts to prepare the acid from *p*-aminobenzoic acid and 2-chlorocyclohexanone were unsuccessful.

m-Aminobenzoic acid (11 g.) and 2-chlorocyclohexanone (5 g.) in ethanol (70 ml.) were boiled for 18 hours and worked up as above to give 1 : 2 : 3 : 4-tetrahydrocarbazole-7-carboxylic acid, m. p. 285—286° (lit., 287°) (0·2 g.) (Found : C, 72·2; H, 6·3. Calc. for $C_{14}H_{13}O_2N$: C, 72·5; H, 6·1%).

Miscellaneous Condensations.—2-Bromocyclohexanone (5 g.) and aniline (10 g.) or *o*- or *p*-toluidine (12·5 g.) gave 1 : 2 : 3 : 4-tetrahydrocarbazole or its 8- or 6-methyl derivative, respectively, in 65%, 55%, and 60% yields.

2-Chloro-5-methylcyclohexanone, b. p. 76—86°/12 mm. (5 g.), was added slowly to boiling aniline (10 g.), and the mixture cooled and treated with dilute hydrochloric acid (100 ml.). The product was extracted with ether, and the extract dried and distilled *in vacuo*. The resulting mixture of methyltetrahydrocarbazoles, b. p. 180—200°/16 mm. (2·4 g., 38%), was crystallised from light petroleum (b. p. 60—80°) to give prisms, m. p. 78—81° (softening at 73°) (Found : C, 83·9; H, 8·0; N, 7·8. Calc. for $C_{13}H_{15}N$: C, 84·3; H, 8·2; N, 7·6%). Dehydrogenation with chloranil gave a mixture of methylcarbazoles, m. p. 219—229°, in 27% yield which on crystallisation from ethanol and purification on a short alumina column gave plates of 2-methylcarbazole, m. p. 241—243°, undepressed on admixture with the authentic carbazole, m. p. 257—259° (Found : C, 85·4; H, 6·1; N, 8·0. Calc. for $C_{13}H_{11}N$: C, 86·2; H, 6·1; N, 7·7%). It formed a picrate, m. p. 161—163° (lit., 167°).

Substituted 2-Anilinocyclohexanones.—These substances were prepared by the method exemplified below. Anhydrous sodium carbonate (3 g.), 2-chlorocyclohexanone (5 g.), *p*-chloroaniline (6 g.), and ethanol (20 ml.) were boiled for 5 hours and then filtered, and the volume of the filtrate reduced. 2-*p*-*Chloroanilinocyclohexanone* separated and crystallised from ethanol in prisms, m. p. 132—134° (44%) (Found : C, 64·8; H, 6·5. $C_{12}H_{14}ONCl$ requires C, 64·4; H, 6·3%). The amino-ketone (0·5 g.) and *p*-chloroaniline hydrochloride (2 g.) were heated in an oil-bath at 250° for 1 hour. The semi-solid product was thoroughly extracted with ether and filtered. The filtrate was washed with dilute hydrochloric acid, water, and sodium carbonate, dried (Na_2SO_4), and evaporated. 6-Chlorotetrahydrocarbazole separated and crystallised from ethanol in colourless plates, m. p. 140—143° (22%). Boiling *o*-chloroaniline (5 g.), 2-chlorocyclohexanone (7·8 g.), and sodium carbonate (3·1 g.) in ethanol (20 ml.) for 24 hours gave 2-*o*-*chloroanilinocyclohexanone*, purified by distillation, b. p. 190—200°/15 mm., followed by crystallisation from light petroleum (b. p. 40—60°), prisms, m. p. 53—54° (yield, 60%) (Found : Cl, 15·5. $C_{12}H_{14}ONCl$ requires Cl, 15·9%). 2-*p*-*Bromoanilinocyclohexanone* formed elongated prisms (from ethanol), m. p. 143—144° (54%) (Found : Br, 30·8. $C_{12}H_{14}ONBr$ requires Br, 29·9%). Attempts to effect ring-closure of the compound with *p*-bromoaniline or its hydrochloride were unsuccessful, but with aniline hydrochloride at 150° for 30 minutes tetrahydrocarbazole resulted (identified by m. p. and mixed m. p.). 2-*o*-*Bromoanilinocyclohexanone* was purified by removal of the excess of *o*-bromoaniline *in vacuo* (the compound itself undergoes decomposition when distilled) and crystallisation of the residue from ethanol; prisms, m. p. 66—69° (40%) (Found : N, 5·05; Br, 28·4. $C_{12}H_{14}ONBr$ requires N, 5·2; Br, 29·9%). 2-2′ : 4′-*Dichloroanilinocyclohexanone*, similarly purified except that light petroleum was used as solvent, formed prisms, m. p. 81—82° (Found : N, 5·5; Cl, 27·0. $C_{12}H_{13}ONCl_2$ requires N, 5·4; Cl, 27·5%).

2-*o*-Chloroanilinocyclohexanone (or the corresponding *p*-bromo-compound) (0·6 g.) and 2 : 4-dinitrophenylhydrazine (0·5 g.) in ethanol containing sulphuric acid were condensed by Brady's method, and the suspension boiled for 2 hours to ensure complete reaction. cyclo*Hexane*-1 : 2-*dione* 2 : 4-*dinitrophenylosazone* was obtained as a scarlet compound which after trituration with boiling glacial acetic acid had m. p. 233—234° (decomp.) (Found : N, 23·1; Cl, 0·0. $C_{18}H_{16}O_4N_8$ requires N, 23·7%). 2-Chlorocyclohexanone and 2 : 4-dinitrophenylhydrazine in ethanol gave by Allen's method (*J. Amer. Chem. Soc.*, 1930, **52**, 2955) the 2 : 4-*dinitrophenylhydrazone*, orange prisms (from tetralin), m. p. 158° (decomp.) (Found : N, 18·3; Cl, 10·9. $C_{12}H_{13}O_4N_4Cl$ requires N, 17·9; Cl, 11·3%). This substance when heated with acetic acid (2 ml.) and water (3 drops) gave a red oil which yielded scarlet crystals, m. p. 233—234° (Found : C, 45·7; H, 3·5; N, 24·3. Calc. for $C_{18}H_{16}O_4N_8$: C, 45·7; H, 3·4; N, 23·7%). This proved

to be the above osazone, and was also obtained by boiling the above dinitrophenylhydrazone or *cyclo*hexane-1 : 2-dione with 2 : 4-dinitrophenylhydrazine in glacial acetic acid.

ω-Chloroacetophenone by Allen's method gave the 2 : 4-dinitrophenylhydrazone, orange needles, m. p. 214—215° (decomp.) (lit., 212°), unaltered when boiled with 2 : 4-dinitrophenylhydrazine and glacial acetic acid for 26 hours. The dinitrophenylhydrazone (0·15 g.) was dissolved in a mixture of water (5 drops) and enough glacial acetic acid to give complete solution at the b. p. After 20 hours, further portions of the dinitrophenylhydrazone (0·15 g.), water (1 ml.), and glacial acetic acid were added, and the solution was boiled for 48 hours. *Phenylglyoxal bis-2 : 4-dinitrophenylhydrazone* separated in scarlet needles, m. p. 296—297° (0·11 g.), from the boiling solution (Found: C, 48·3; H, 3·3; N, 21·6. $C_{20}H_{14}O_8N_8$ requires C, 48·0; H, 2·8; N, 22·6%).

Thanks are expressed to the Department of Scientific and Industrial Research for the award of a maintenance grant to one of us (E. B. McC.), and to Dr. E. G. V. Percival for helpful advice.

UNIVERSITY OF EDINBURGH. [*Received, June 5th*, 1950.]

---

559. *Intramolecular Acylation. Part II. The Ring Closure of Some α-Substituted Glutaric Acids.*

By M. F. ANSELL and D. H. HEY.

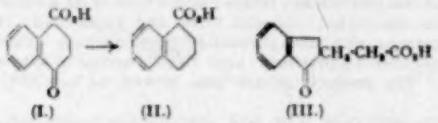
Intramolecular acylation of the nine α-substituted glutaric acids having the formula R·CH(CO$_2$H)·CH$_2$·CH$_2$·CO$_2$H, R·CH$_2$·CH(CO$_2$H)·CH$_2$·CH$_2$·CO$_2$H, and R·CH$_2$·CH$_2$·CH(CO$_2$H)·CH$_2$·CH$_2$·CO$_2$H, in which in each case R is phenyl, α- and β-naphthyl, has been effected by the use of anhydrous hydrogen fluoride, and the constitutions of the ketonic acids thus obtained have been established as follows. Both 1-ketotetralin-4-carboxylic acid (I) and -2-β-propionic acid (IV) have been converted into the corresponding non-ketonic acids (II and V) by Clemmensen reduction and, in addition, (IV) has been converted successively into the lactone of 1-hydroxy-1 : 2 : 3 : 4-tetrahydronaphthalene-2-β-propionic acid (VII) and 4 : 5-benzindan-3-one (VIII). 1-Keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-4-carboxylic (XI) and -2-β-propionic acid (XVIII), 4-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-1-carboxylic (XXIV) and -3-β-propionic acid (XXVI) have been reduced to the corresponding non-ketonic acids and thence converted into known reference compounds. Both 1- (XV) and 3-keto-4 : 5-benzindane-2-β-propionic acid (XVII) have been converted similarly into 4 : 5-benzindane-2-β-propionic acid (XVI). Further, (XVIII) has been converted successively into the lactone of 1-hydroxy-1 : 2 : 3 : 4-tetrahydrophenanthrene-2-β-propionic acid (XXII) and 1'-keto-1 : 2-*cyclo*pentenophenanthrene (XXI), a compound also obtained by the action of anhydrous hydrogen fluoride on phenanthrene-2-β-propionic acid (XX).

THE development of a new method of preparation (Ansell and Hey, *J.*, 1950, 1683) has rendered available a number of α-substituted glutaric acids, which are suitable starting compounds for the preparation of polycyclic systems by intramolecular acylation. The present communication is devoted to a study of the ring closure of the nine α-substituted glutaric acids having the formulæ R·CH(CO$_2$H)·CH$_2$·CH$_2$·CO$_2$H, R·CH$_2$·CH(CO$_2$H)·CH$_2$·CH$_2$·CO$_2$H, and R·CH$_2$·CH$_2$·CH(CO$_2$H)·CH$_2$·CH$_2$·CO$_2$H, where in each case R is phenyl, α- and β-naphthyl. Anhydrous hydrogen fluoride was chosen as the reagent most likely to yield satisfactory results as regards yields, purity of product, and ease of manipulation (cf. Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1939, **61**, 1272), but alternative methods of cyclisation have been employed in some instances, either for purposes of comparison or when the hydrogen fluoride method was unsatisfactory. The results show that it is possible to obtain relatively complex polycyclic systems in a straightforward manner from easily accessible starting compounds, and new routes are thus opened up for the synthesis of a variety of polycyclic structures of current interest. This method, as applied to suitably substituted dicarboxylic acids in general, has received only limited application in the past (cf. von Braun, Bayer, and Cassel, *Ber.*, 1927, **60**, 2602; von Braun and Irmisch, *Ber.*, 1931, **64**, 2461; von Braun and Weissbach, *ibid.*, p. 1785; Manske, *J. Amer. Chem. Soc.*, 1931, **53**, 1104; Ramage and Robinson, *J.*, 1933, 607; Ramage, *J.*, 1938, 397, etc.). The action of anhydrous hydrogen fluoride on some β-substituted glutaric acids has been described in Part I (Hey and Kohn, *J.*, 1949, 3177).

The action of anhydrous aluminium chloride on α-phenylglutaryl chloride in carbon disulphide solution gave 1-ketotetralin-4-carboxylic acid (I) in 60% yield, but when the free acid was treated with anhydrous hydrogen fluoride 71% of the starting material was recovered unchanged and the yield of (I) was reduced to 17%. Since the completion of this work Horning and Finelli (*J. Amer. Chem. Soc.*, 1949, **71**, 3204) have reported the formation of (I) in 57% yield by the action of concentrated sulphuric acid on α-phenylglutaric anhydride. When, however, these workers treated α-phenylglutaric anhydride with aluminium bromide in benzene solution,

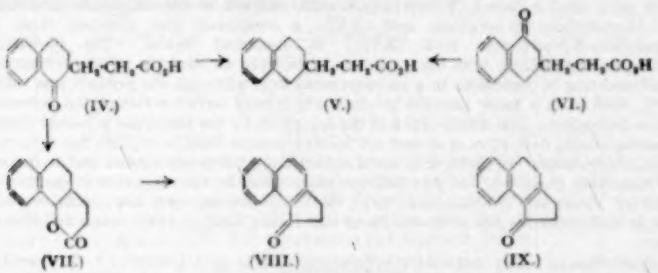
intermolecular acylation took place with formation of γ-benzoyl-α-phenylbutyric acid. The structure of 1-ketotetralin-4-carboxylic acid was confirmed by its conversion, on Clemmensen reduction, into 1 : 2 : 3 : 4-tetrahydro-1-naphthoic acid (II) (Baeyer and Schoder, *Annalen*, 1891, **266**, 184; Newman and O'Leary, *J. Amer. Chem. Soc.*, 1946, **68**, 258). The poor yield of 1-ketotetralin-4-carboxylic acid obtained by the action of anhydrous hydrogen fluoride on α-phenylglutaric acid illustrates the resistance to ring closure encountered by Badger, Campbell, and Cook (*J.*, 1949, 1084) in the case of the α-phenyl nucleus in αβ-diphenylglutaric acid. Other examples in which hydrogen fluoride gives less satisfactory results than aluminium chloride have been reported by Hey and Kohn (*loc. cit.*).

The formation of 1-ketoindane-2-β-propionic acid (III) in 30% yield by the action of aluminium chloride on α-benzylglutaric anhydride in nitrobenzene solution has been reported by von Braun and Manz (*Annalen*, 1929, **468**, 258) and it is now shown that the same compound is formed in 81% yield by the action of anhydrous hydrogen fluoride on free α-benzylglutaric acid.



(I.) (II.) (III.)

The action of cold 98% sulphuric acid on α-(2-phenylethyl)glutaric acid gave 1-ketotetralin-2-β-propionic acid (IV) in a yield of 90%, and the yield with anhydrous hydrogen fluoride was 86·5%. The structure of (IV) was established by Clemmensen reduction to tetralin-2-β-propionic acid (V), prepared previously by von Braun, Bayer, and Cassel (*loc. cit.*) by the similar reduction of 1-ketotetralin-3-β-propionic acid (VI).

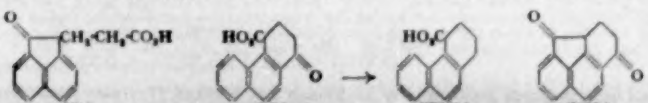


(IV.) (V.) (VI.)

(VII.) (VIII.) (IX.)

An attempt to prepare the 2 : 4-dinitrophenylhydrazone of (IV) by Brady's method (*J.*, 1931, 757) gave the 2 : 4-dinitrophenylhydrazone of the ethyl ester. Esterification of the carboxyl group in keto-acids under Brady's conditions has previously been reported by Cowley and Schuette (*J. Amer. Chem. Soc.*, 1933, **55**, 3465) and by Strain (*ibid.*, 1935, **57**, 758). Reduction of the keto-acid (IV) with sodium amalgam gave the lactone of 1-hydroxytetralin-2-β-propionic acid (VII) which, when heated with phosphoric oxide in xylene solution, gave a non-acidic product which proved to be 4 : 5-benzindan-3-one (VIII) and not the expected 6 : 7-dihydro-compound (IX). An authentic sample of (VIII) was prepared for purposes of comparison by the cyclisation of naphthalene-2-β-propionic acid, obtained in turn by the hydrolysis of ethyl 2-naphthylmethylmalonate, as described by Mayer and Sieglitz (*Ber.*, 1922, **55**, 1835). This cyclisation was effected in 96% yield by using anhydrous hydrogen fluoride (cf. Cook and Hewett, *J.*, 1933, 1111).

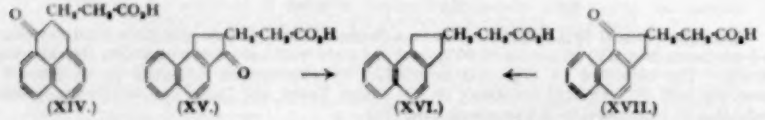
Cyclisation of α-1-naphthylglutaric acid can give rise to three possible products (X, XI, XII)



(X.) (XI.) (XIII.) (XII.)

in addition to a compound containing a seven-membered ring. The product obtained by the use of anhydrous hydrogen fluoride contained only acidic material, which eliminates compound (XII), and the sole product (95% yield) consisted of 1-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-4-carboxylic acid (XI). Reduction of the product by Huang-Minlon's modification of the Wolff–Kishner reaction (*J. Amer. Chem. Soc.*, 1946, **68**, 2487) gave 1 : 2 : 3 : 4-tetrahydrophenanthrene-4-carboxylic acid (XIII) (m. p. 145—146°), whereas similar reduction of (X) would have given acenaphthene-7-β-propionic acid (m. p. 108·5—109·5°; Bachmann and Sheehan, *ibid.*, 1941, **63**, 204). The structure (XI) was confirmed by the identification of 1 : 2 : 3 : 4-tetrahydrophenanthrene as a by-product of the reduction, and also by the formation of phenanthrene when the 1 : 2 : 3 : 4-tetrahydrophenanthrene-4-carboxylic acid was heated with palladium–charcoal. Attempts to dehydrogenate this acid with sulphur always gave a slightly impure product, but similar dehydrogenation of the methyl ester gave a product from the hydrolysis of which pure phenanthrene-4-carboxylic acid was obtained.

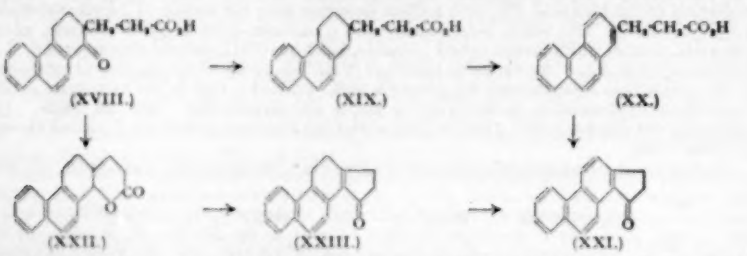
Treatment of α-1-naphthylmethylglutaric acid with anhydrous hydrogen fluoride gave a tar from which a single ketonic product was isolated in the form of its semicarbazone in only 22% yield. This result was unexpected, although Fieser and Jones (*ibid.*, 1942, **64**, 1666) have reported a similar experience with acenaphthene-3-β-propionic acid. This reaction could give rise to 7-ketoperinaphthane-8-β-propionic acid (XIV) and/or 1-keto-4 : 5-benzindane-2-β-propionic acid (XV). The product isolated was proved to be (XV) by the facts that



(XIV.) (XV.) (XVI.) (XVII.)

oxidation gave naphthalene-1 : 2-dicarboxylic acid, isolated as the anhydride, and reduction gave 4 : 5-benzindane-2-β-propionic acid (XVI), a compound also obtained from 3-keto-4 : 5-benzindane-2-β-propionic acid (XVII) as described below. The cyclisation of α-1-naphthylmethylglutaric acid thus appears to provide an example of the formation of a five-membered ring in preference to a six-membered ring, although the product was isolated in only 22% yield from a tarry reaction product which may have contained the isomeric perinaphthane derivative. The deactivation of the 8-position by the side chain is hardly likely, and, if the perinaphthane derivative is in fact not formed, a more feasible explanation is to be found in steric considerations. In the cyclisation of naphthalene-1-β-propionic acid and its derivatives, in most cases ring closure at the *peri*-position takes place to the exclusion of reaction at the 2-position (cf. Fieser and Novello, *ibid.*, 1940, **62**, 1855), but examples are also known in which reactions at both positions are involved (Fieser and Gates, *ibid.*, p. 2335; Cook and Hewett, *J.*, 1934, 365).

The cyclisation of α-(2-1′-naphthylethyl)glutaric acid to give 1-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-2-β-propionic acid (XVIII) was accomplished in a yield of 65% with hot 85% sulphuric acid, and in a yield of 92·5% with anhydrous hydrogen fluoride. The structure of the product was established by Clemmensen reduction to 1 : 2 : 3 : 4-tetrahydrophenanthrene-2-β-propionic acid (XIX), followed by dehydrogenation to phenanthrene-2-β-propionic acid (XX)



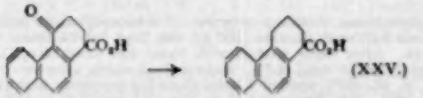
(XVIII.) (XIX.) (XX.) (XXII.) (XXIII.) (XXI.)

which had been prepared previously by Bachmann and Kloetzel (*J. Amer. Chem. Soc.*, 1937, **59**, 2307) by the reduction of phenanthrene-2-β-acrylic acid. The action of anhydrous hydrogen

fluoride on phenanthrene-2-β-propionic acid (XX) gave 1'-keto-1 : 2-*cyclo*pentenophenanthrene (XXI) in a yield of 80%, whereas Bachmann and Kloetzel (*loc. cit.*) have reported that by the action of stannic chloride on phenanthrene-2-β-propionyl chloride the ketocyclopentenophenanthrene is obtained in only 54% yield.

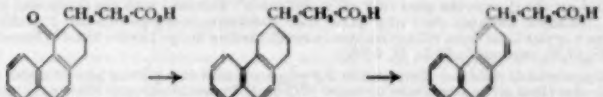
Reduction of 1-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-2-β-propionic acid (XVIII) with sodium amalgam gave the lactone (XXII) of the 1-hydroxy-acid, which with phosphoric oxide in boiling xylene gave a neutral product; this is considered to be 1'-keto-1 : 2-*cyclo*penteno-3 : 4-dihydrophenanthrene (XXIII), because on dehydrogenation it gave 1'-keto-1 : 2-*cyclo*pentenophenanthrene (XXI), identical with the product obtained as described above.

The action of anhydrous hydrogen fluoride on α-2-naphthylglutaric acid gave 4-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-1-carboxylic acid (XXIV) in 71% yield. The structure of the latter was proved by the fact that on reduction by the Huang-Minlon modification of the Wolff–Kishner method both 1 : 2 : 3 : 4-tetrahydrophenanthrene and 1 : 2 : 3 : 4-tetrahydrophenanthrene-1-carboxylic acid (XXV) were obtained.



(XXIV.) (XXV.)

Treatment of α-2-naphthylmethylglutaric acid with anhydrous hydrogen fluoride gave 3-keto-4 : 5-benzindane-2-β-propionic acid (XVII) in 92% yield. Oxidation of the latter gave naphthalene-1 : 2-dicarboxylic acid, whereas Clemmensen reduction gave 4 : 5-benzindane-2-β-propionic acid (XVI), which was also obtained similarly from the isomeric keto-acid (XV) as reported above. Formation of the same end-product from both α-1- and α-2-naphthylmethylglutaric acid provides further evidence that the five-membered ring must be attached to the naphthalene nucleus at the 1- and the 2-positions.



(XXVI.) (XXVII.) (XXVIII.)

The action of anhydrous hydrogen fluoride on α-(2-2'-naphthylethyl)glutaric acid gave 4-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-3-β-propionic acid (XXVI) in 64% yield. The structure of the latter was proved by Wolff–Kishner reduction to 1 : 2 : 3 : 4-tetrahydrophenanthrene-3-β-propionic acid (XXVII), which in turn was dehydrogenated to give phenanthrene-3-β-propionic acid (XXVIII) (Bachmann and Kloetzel, *loc. cit.*).

Experimental.

In the reactions with anhydrous hydrogen fluoride "Polythene" beakers were used and the reactions were carried out in the open under shelter.

1-Ketotetralin-4-carboxylic Acid.—(*a*) A solution of α-phenylglutaric acid (4·5 g.) (Ansell and Hey, *loc. cit.*) in anhydrous hydrogen fluoride (100 g.) was set aside at 15—20° for 18 hours and then poured on crushed ice. The sticky solid which separated was extracted with ether and washed with water. Evaporation of the dried ethereal extract left a viscous oil (4·4 g.), which was dissolved in alcohol (10 c.c.) and heated at 75° for 1 hour with semicarbazide hydrochloride (4·0 g.) in a mixture of alcohol (30 c.c.) and pyridine (4 c.c.). Fine needle-like crystals rapidly separated. Next morning, filtration gave *1-ketotetralin-4-carboxylic acid semicarbazone* (0·83 g.), m. p. 230° after recrystallisation from ethoxyethanol (Found: C, 58·0; H, 5·4. $C_{12}H_{15}O_3N_3$ requires C, 58·3; H, 5·3%). The mother-liquors from the semicarbazone were made strongly acid with hydrochloric acid and extracted with ether. The ethereal extract was washed with 2*N*-hydrochloric acid and water. Evaporation of the dried extract left α-phenylglutaric acid (3·2 g.) as an oil which readily solidified and had m. p. and mixed m. p. 82—84° after recrystallisation from ice-cold benzene–light petroleum (b. p. 40—60°). The semicarbazone (0·515 g.) was hydrolysed by boiling it under reflux with 20% hydrochloric acid (100 c.c.) for 30 minutes; the mixture was cooled and extracted with ether. The extract was washed with water, dried, and evaporated, to give *1-ketotetralin-4-carboxylic acid* (0·342 g.) as an oil, which readily solidified. Recrystallisation from benzene–light petroleum (b. p. 40—60°) gave the pure acid in glistening plates, m. p. 94—95° (Found: C, 69·4; H, 5·2. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·3%). Horning and Finelli (*loc. cit.*), after the completion of this work, recorded m. p. 93—95°.

(*b*) α-Phenylglutaryl chloride was prepared from α-phenylglutaric acid (5·2 g.) and phosphorus pentachloride (10·5 g.) in dry thiophen-free benzene (10 c.c.). After distillation under reduced pressure to remove benzene and phosphorus oxychloride and pentachloride, the residue of α-phenylglutaryl chloride

was dissolved in carbon disulphide (15 c.c.) and added to an ice-cold stirred suspension of anhydrous aluminium chloride (5·5 g.) in carbon disulphide (15 c.c.). After being kept at 0° for 1 hour, the mixture was stirred at room temperature for 2 hours. The carbon disulphide was removed under reduced pressure and the residue cooled to 0° and decomposed with ice and hydrochloric acid. The acid solution was extracted with ether, and the extract washed with 2*N*-hydrochloric acid and water and dried. Evaporation left a reddish oil (4·5 g.), which was converted into the semicarbazone (3·5 g.; m.p. 228—229°) and thence into the free keto-acid (2·5 g.) as described above. When purified as described above, this had m. p. 94—95° and was identical with that obtained by method (*a*).

1 : 2 : 3 : 4-*Tetrahydro*-1-*naphthoic Acid*.—1-Ketotetralin-4-carboxylic acid (1·0 g.) was added to a suspension of amalgamated zinc (5·0 g.) in a mixture of water (3 c.c.), concentrated hydrochloric acid (9 c.c.), glacial acetic acid (0·3 c.c.), and toluene (5 c.c.). The mixture was boiled under reflux for 24 hours, during which time a further quantity of hydrochloric acid (10 c.c.) was added. The toluene layer was then separated, the aqueous layer extracted with ether, and the combined toluene and ether extracts were washed with water. The residual oil, obtained on removal of the solvents from the dried extract, was distilled to yield 1 : 2 : 3 : 4-tetrahydro-1-naphthoic acid (0·6 g.), b. p. 110—112°/0·5 mm., which immediately solidified. Recrystallisation from ethyl acetate gave the acid in colourless prisms, m. p. 82—84°. Newman and O'Leary (*loc. cit.*) record m. p. 80—81° and Baeyer and Schoder (*loc. cit.*) m. p. 85°.

1-*Ketoindane*-2-β-*propionic Acid*.—A solution of α-benzylglutaric acid (5·0 g.) (Ansell and Hey, *loc. cit.*) in anhydrous hydrogen fluoride (100 g.) was kept for 24 hours, and then poured on ice and extracted with ether. After being washed with water and dried (Na_2SO_4), the ethereal solution was evaporated. A slightly yellow solid (4·5 g.) was obtained which, after two crystallisations from benzene–light petroleum (b. p. 40—60°), yielded 1-ketoindane-2-β-propionic acid (3·7 g.) in small, pale yellow, needles, m. p. 106—108°. von Braun and Manz (*loc. cit.*) record m. p. 103—105°.

1-*Ketotetralin*-2-β-*propionic Acid*.—(*a*) A solution of α-(2-phenylethyl)glutaric acid (21·0 g.) (Ansell and Hey, *loc. cit.*) in 98% sulphuric acid (110 c.c.) was kept at room temperature for 24 hours and then poured on ice. The precipitated *keto-acid* (17·4 g.; m. p. 96—99°) was collected and washed with water. Recrystallisation from water–dioxan (3 : 1) gave the pure acid in small needles, m. p. 107—108° (Found: C, 71·4; H, 6·2. $C_{13}H_{14}O_3$ requires C, 71·6; H, 6·4%).

(*b*) A solution of α-(2-phenylethyl)glutaric acid (5·0 g.) in anhydrous hydrogen fluoride (100 g.) was kept for 24 hours and then poured on ice. The precipitated acid was quickly filtered off, washed with water, and dried, to give 1-ketotetralin-2-β-propionic acid (4·0 g.; m. p. 105—107°). Recrystallisation from water–dioxan (3 : 1) gave the pure acid, m. p. 107—108°, identical with the compound prepared by method (*a*). Brady's method (*loc. cit.*) gave *ethyl* 1-*ketotetralin*-2-β-*propionate* 2 : 4-*dinitrophenylhydrazone*, which crystallised from ethoxyethanol in small needles, m. p. 183·5—184·5° (Found: C, 58·8; H, 5·2. $C_{21}H_{22}O_6N_4$ requires C, 59·2; H, 5·2%).

Tetralin-2-β-*propionic Acid*.—1-Ketotetralin-2-β-propionic acid (5·0 g.) was heated under reflux with amalgamated zinc (10·0 g.) in a mixture of water (7·5 c.c.), hydrochloric acid (17·5 c.c.), glacial acetic acid (0·5 c.c.), and toluene (10 c.c.) for 30 hours, during which more hydrochloric acid (18 c.c.) was added. The product was extracted as recorded for 1 : 2 : 3 : 4-tetrahydro-1-naphthoic acid. Distillation of the oil obtained on evaporation of the dried extract gave tetralin-2-β-propionic acid (3·3 g.), b. p. 188—192°/6 mm., which readily solidified. Recrystallisation from light petroleum (b. p. 40—60°) gave colourless needles, m. p. 72—73°. von Braun, Bayer, and Cassel (*loc. cit.*) record m. p. 73°.

Lactone of 1-*Hydroxy*-*tetralin*-2-β-*propionic acid*. Sodium amalgam (2%; 200 g.) was added to a solution of 1-ketotetralin-2-β-propionic acid (4·0 g.) in 2% aqueous sodium hydroxide (100 c.c.). The mixture was kept warm for 24 hours and the aqueous solution then decanted from the mercury. The mercury was thoroughly washed with water, and the combined aqueous solutions acidified with hydrochloric acid. The oil which separated solidified and was collected by filtration. After being dried *in vacuo* over sulphuric acid, it was distilled to give the *lactone* (3·2 g.), b. p. 155—157°/0·5 mm., of 1-hydroxy-1 : 2 : 3 : 4-tetrahydronaphthalene-2-β-propionic acid. This readily solidified and crystallised from benzene–light petroleum (b. p. 40—60°) in small rod-shaped crystals, m. p. 142—144° (Found: C, 77·2; H, 6·4. $C_{13}H_{14}O_3$ requires C, 77·2; H, 6·9%).

Conversion of the Lactone into 4 : 5-*Benzindan*-3-*one*.—Phosphoric oxide (0·71 g.) was added to a solution of the above lactone (1·0 g.) in xylene (5 c.c.) and the mixture boiled under reflux for 30 minutes. After removal of the xylene, the tarry residue was distilled (b. p. 120—160°/0·5 mm.) and the solid distillate digested with 5% aqueous potassium hydroxide (20 c.c.) on a water-bath for 1 hour. The neutral product was extracted with ether and washed with water. Evaporation of the dried ethereal extract left an oil (0·36 g.), which readily solidified. Recrystallisation from aqueous acetic acid (charcoal) yielded 4 : 5-benzindan-3-one in long colourless needles, m. p. 102·5—103·5°. A mixed m. p. with an authentic specimen, prepared as described below, showed no depression.

4 : 5-*Benzindan*-3-*one*.—A solution of naphthalene-2-β-propionic acid (0·31 g.) (Mayer and Sieglitz, *loc. cit.*) in anhydrous hydrogen fluoride (20 g.) was kept for 24 hours, after which time all the hydrogen fluoride had evaporated. The residue was dissolved in ether and washed with 5% aqueous sodium carbonate and with water. Evaporation of the dried extract left 4 : 5-benzindan-3-one (0·28 g.) in slightly yellow needles, m. p. 96—99°. Recrystallisation from aqueous acetic acid (charcoal) gave the compound in long colourless needles, m. p. 102·5—103·5°. Mayer and Sieglitz (*loc. cit.*) give m. p. 103°, and Cook and Hewett (*J.*, 1933, 1111) m. p. 102—103°.

1-*Keto*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*-4-*carboxylic Acid*.—A solution of α-1-naphthylglutaric acid (10·0 g.) (Ansell and Hey, *loc. cit.*) in anhydrous hydrogen fluoride (200 g.) was set aside for 24 hours and then poured on ice. The precipitated solid was quickly filtered off, washed with water, and dissolved in 5% aqueous sodium carbonate (100 c.c.). After extraction with ether the solution was treated with

charcoal and filtered. Evaporation of the dried ethereal extract left no residue. The acid precipitated on acidification of the alkaline solution was filtered off, washed with water, and dried (5·8 g.; m. p. 190—198°). Recrystallisation from benzene (800 c.c.) gave *1-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-4-carboxylic acid* (7·3 g.) in rhomboheda, m. p. 198—200° (decomp.) (Found: C, 74·9; H, 5·0. $C_{15}H_{12}O_3$ requires C, 75·0; H, 5·0%). A further 0·8 g., m. p. 190—198°, was obtained on concentration of the mother-liquors.

1 : 2 : 3 : 4-*Tetrahydrophenanthrene-4-carboxylic Acid.*—A mixture of the foregoing acid (2·4 g.), potassium hydroxide (1·9 g.), 85% hydrazine hydrate (2 c.c.), and diethylene glycol (15 c.c.) was boiled under reflux for 1½ hours (*cf.* Huang-Minlon, *loc. cit.*). The solution was then distilled until the internal temperature reached 195°, and then heated under reflux for 4 hours (bath-temp. 220—240°). After cooling, the solution was diluted with water (15 c.c.) and poured into 6*N*-hydrochloric acid (10 c.c.) The oil which separated was extracted with ether. The extract was washed with 5% aqueous sodium carbonate, and the alkaline washings were acidified with 2*N*-hydrochloric acid and again extracted with ether. Evaporation (after drying) of the first ethereal extract left 1 : 2 : 3 : 4-tetrahydrophenanthrene (0·4 g.; m. p. 28—30°), identified by the m. p. and mixed m. p. of its picrate with an authentic specimen (m. p. 111·5°) prepared by the method of Bachmann and Struve (*J. Org. Chem.*, 1939, **4, 472). Evaporation (after drying) of the second ethereal extract left *1 : 2 : 3 : 4-tetrahydrophenanthrene-4-carboxylic acid* (1·5 g.), m. p. 135—145°. Further recrystallisation from light petroleum (b. p. 80—100°) containing a little benzene gave the acid in long thin plates (1·25 g.), m. p. 145—146° (Found: C, 80·0; H, 6·0. $C_{15}H_{14}O_2$ requires C, 79·7; H, 6·2%). The *methyl* ester, prepared by diazomethane, crystallised from ice-cold methyl alcohol in colourless prisms, m. p. 57—58° (Found: C, 80·4; C, 6·6. $C_{16}H_{14}O_2$ requires C, 80·0; H, 6·7%).

Dehydrogenation of **1 : 2 : 3 : 4-*Tetrahydrophenanthrene-4-carboxylic Acid.*—The tetrahydro-acid (0·3 g.) was heated to 200° with 10% palladium-charcoal (0·1 g.) for 15 minutes. A further 0·1 g. of catalyst was then added and heating continued at 240° for a further 7½ hours. During this time 100 c.c. of gas was evolved. The reaction mixture was thoroughly extracted with ether, and after filtration the ethereal extract was washed with 5% aqueous sodium carbonate. Acidification of the alkaline solution yielded only a trace of material, but evaporation of the dried ethereal extract gave phenanthrene (0·3 g.), identified by the m. p. and mixed m. p. of its picrate (m. p. 143—144° from alcohol).

Dehydrogenation of Methyl **1 : 2 : 3 : 4-*Tetrahydrophenanthrene-4-carboxylate.*—A mixture of the ester (0·2 g.) and sulphur (0·533 g.) was heated at 240—250° for 3 hours. The reaction mixture was then hydrolysed by boiling aqueous sodium hydroxide (10 c.c.; 20%) for 2 hours. After extraction with ether, the solution was treated with charcoal and filtered. Acidification of the filtrate gave phenanthrene-4-carboxylic acid (0·02 g.), m. p. 167—169°. Recrystallisation from aqueous acetic acid gave the pure acid, m. p. 169—171°. Fieser, Fieser, and Hershberg (*J. Amer. Chem. Soc.*, 1936, **58**, 2325) record m. p. 171·5—173°, and Kruber (*Ber.*, 1934, **67**, 1000) records m. p. 170—171°.

1-Keto-4 : 5-benzindane-2-β-propionic Acid.—A solution of α-1-naphthylmethylglutaric acid (5·0 g.) (Ansell and Hey, *loc. cit.*) in anhydrous hydrogen fluoride (100 g.) was kept for 24 hours and then poured on ice. A dark greenish-brown oil separated, which was extracted with ether and washed with water. Evaporation of the dried ethereal extract left a dark oil, which was dissolved in hot alcohol (30 c.c.) (charcoal), and the solution was cooled and filtered. The resulting pale yellow solution was heated at 75° for 1 hour with a solution of semicarbazide hydrochloride (3·0 g.) in a mixture of alcohol (10 c.c.) and pyridine (4 c.c.). A pale yellow, highly insoluble semicarbazone rapidly separated, which after cooling was filtered off and dried (1·7 g.; m. p. 240—244°). The free ketone was regenerated by boiling the semicarbazone with 20% hydrochloric acid (150 c.c.) for 1½ hours and then extracted with ether. After being washed with water and dried, the ethereal solution was evaporated to give *1-keto-4 : 5-benzindane-2-β-propionic acid* (1·0 g.) as an oil, which readily solidified and then had m. p. 97—100°. Recrystallisation from benzene–light petroleum (b. p. 40—60°), in the presence of activated alumina, yielded the pure acid in clusters of small needles, m. p. 103·5—104·5° (Found: C, 75·3; H, 5·3. $C_{14}H_{14}O_3$ requires C, 75·6; H, 5·5%).

**4 : 5-*Benzindane-2-β-propionic Acid.*—The above keto-acid (0·8 g.), amalgamated zinc (2·5 g.), water (2 c.c.), concentrated hydrochloric acid (5 c.c.), glacial acetic acid (2 drops), and toluene (2·5 c.c.) were boiled under reflux for 24 hours, during which a further quantity (3 c.c.) of hydrochloric acid was added, and then extracted as for 1 : 2 : 3 : 4-tetrahydro-1-naphthoic acid. The oil obtained on evaporation of the dried extracts was distilled at 0·1 mm. (bath-temp. 220°) to give 4 : 5-benzindane-2-β-propionic acid (0·3 g.) as an oil, which readily solidified. Recrystallisation from benzene–light petroleum (b. p. 60—80°) gave the acid in clusters of small needles, m. p. 106—107°, raised to 107—108° on admixture with an authentic specimen (m. p. 107—108°) obtained by the reduction of 3-keto-4 : 5-benzindane-2-β-propionic acid (see below).

Oxidation of **1-*Keto-4 : 5-benzindane-2-β-propionic Acid.*—A cold saturated aqueous solution of potassium permanganate was added to a solution of 1-keto-4 : 5-benzindane-2-β-propionic acid (0·4 g.) in 10% aqueous sodium hydroxide (10 c.c.) until the violet colour persisted. It was then decolourised by the addition of sodium sulphite, the precipitated manganese dioxide filtered off, and dilute sulphuric acid added. After being boiled for a short time to remove sulphur dioxide, the solution was cooled and extracted with ether. Evaporation of the ethereal extract left an oil, from which the anhydride of naphthalene-1 : 2-dicarboxylic acid sublimed under reduced pressure at 180—200° (bath-temp.). Recrystallisation from light petroleum (b. p. 60—80°) gave the anhydride in small needles, m. p. 165—167. A mixed m. p. with the anhydride (m. p. 167—168°) obtained by the oxidation of 3-keto-4 : 5-benzindane-2-β-propionic acid (see below) showed no depression.

**1-*Keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-2-β-propionic Acid.*—(*a*) A solution of α-(2-1′-naphthylethyl)glutaric acid (1·0 g.) (Ansell and Hey, *loc. cit.*) in 85% sulphuric acid (4 c.c.) was heated on a water-bath for 1 hour, cooled, and poured on ice. The precipitated acid was filtered off, washed with water, and

dried to give 1-*keto*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*-2-β-*propionic acid* (0·75 g.), m. p. 142—145°. Recrystallisation from dioxan–water (1 : 3) gave the pure acid in small colourless needles, m. p. 143—146° (Found: C, 75·7; H, 5·8. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%). (*b*) A solution of α-(2-1′-naphthylethyl)glutaric acid (3·0 g.) in anhydrous hydrogen fluoride (60 g.) was kept for 24 hours and then poured on ice. The precipitated solid was collected, washed with water, and dried, to give 1-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-2-β-propionic acid (2·6 g.), m. p. 143—146°, identical with that prepared by method (*a*).

1 : 2 : 3 : 4-*Tetrahydrophenanthrene*-2-β-*propionic Acid*.—The foregoing acid (4·0 g.), amalgamated zinc (10·0 g.), water (7·5 c.c.), hydrochloric acid (17·5 c.c.), glacial acetic acid (0·5 c.c.), and toluene (10 c.c.) were boiled under reflux for 24 hours, during which a further quantity of hydrochloric acid (18 c.c.) was added. The mixture was then extracted as for 1 : 2 : 3 : 4-tetrahydro-1-naphthoic acid. Distillation of the oil obtained on evaporation of the extracts gave 1 : 2 : 3 : 4-*tetrahydrophenanthrene*-2-β-*propionic acid* (2·2 g.), b. p. 191—196°/0·008 mm., which immediately solidified. Recrystallisation from benzene gave the compound in clusters of small needles, m. p. 148·5—149·5° (Found: C, 80·5; H, 7·2. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%).

Phenanthrene-2-β-*propionic Acid*.—A mixture of 1 : 2 : 3 : 4-tetrahydrophenanthrene-2-β-propionic acid (0·508 g.) and sulphur (0·128 g.) was heated at 220—250° for 2 hours. When cold, the reaction mixture was digested with 5% aqueous sodium hydroxide (30 c.c.), treated with charcoal, and filtered. Acidification of the filtrate gave crude phenanthrene-2-β-propionic acid (0·22 g.), m. p. 160—176°. Two recrystallisations from aqueous acetic acid gave the pure acid in small needles, m. p. 177—177·5°. Bachmann and Kloetzel (*loc. cit.*) record m. p. 177—177·5°.

1′-*Keto*-1 : 2-*cyclopentanophenanthrene*.—A solution of phenanthrene-2-β-propionic acid (0·15 g.) in anhydrous hydrogen fluoride (20 g.) was kept for 24 hours, after which all the hydrogen fluoride had evaporated. The residue was extracted with ether and washed with 5% aqueous sodium carbonate and water. Evaporation of the dried ethereal solution left needles of 1′-keto-1 : 2-*cyclo*pentenophenanthrene (0·111 g.), m. p. 181—184°. Sublimation at 200° (bath-temp.)/0·3 mm., followed by recrystallisation from acetic acid, raised the m. p. to 183—184°. Bachmann and Kloetzel (*loc. cit.*) record m. p. 184°.

Lactone of 1-*Hydroxy*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*-2-β-*propionic Acid*.—Sodium amalgam (2%; 100 g.) was added to a solution of 1-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-2-β-propionic acid (2·0 g.) in 2% aqueous sodium hydroxide (50 c.c.). The mixture was kept warm for 24 hours and the aqueous layer decanted from the mercury. The mercury was thoroughly washed with water and the combined aqueous solutions acidified, an oil separating. After decantation of the aqueous layer the oil was treated with ether, whereupon it solidified. The solid product, together with a small amount of material obtained on evaporation of the ethereal solution, was distilled to give the 1-*hydroxy*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*-2-β-*propionic acid lactone* (1·3 g.), b. p. 215—220°/0·15 mm., which immediately solidified. Recrystallisation from benzene gave the lactone in clusters of small needles, m. p. 147—148° (Found: C, 80·8; H, 6·2. $C_{17}H_{14}O_2$ requires C, 81·0; H, 6·3%).

1′-*Keto*-3 : 4-*dihydro*-1 : 2-*cyclopentanophenanthrene*.—Phosphoric oxide (1·4 g.) was added to a solution of the above lactone (2·5 g.) in xylene (10 c.c.), and the mixture was boiled under reflux for 1 hour. The xylene was removed under reduced pressure and the residue digested with 5% aqueous sodium hydroxide (50 c.c.) for 1 hour on a water-bath. The neutral product was extracted with ether and washed with water. Evaporation of the dried ethereal extract left a brown oil which solidified. Sublimation at 170—180°/0·3 mm. gave 1′-*keto*-3 : 4-*dihydro*-1 : 2-*cyclopentanophenanthrene* (0·5 g.), which crystallised from benzene in colourless needles, m. p. 165—166° (Found: C, 86·9; H, 6·0. $C_{17}H_{14}O$ requires C, 87·2; H, 6·0%).

Dehydrogenation of 1′-*Keto*-3 : 4-*dihydro*-1 : 2-*cyclopentanophenanthrene*.—The ketone (0·055 g.) and sulphur (0·0075 g.) were heated at 230—240° (bath-temp.) for 1½ hours. From the reaction mixture 1′-keto-1 : 2-*cyclo*pentenophenanthrene was isolated by sublimation at 200°/0·3 mm. Recrystallisation from aqueous acetic acid gave the compound as pale yellow needles, m. p. 181—184°. A mixed m. p. with 1′-keto-1 : 2-*cyclo*pentenophenanthrene, m. p. 183—184°, prepared from phenanthrene-2-β-propionic acid as described above, showed no depression.

4-*Keto*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*-1-*carboxylic Acid*.—A solution of α-2-naphthylglutaric acid (3·5 g.) (Ansell and Hey, *loc. cit.*) in anhydrous hydrogen fluoride (70 g.) was kept for 24 hours and then poured on ice. The viscous oil which separated was extracted with ether and washed with water. Evaporation of the dried ethereal extract left an oil (3·0 g.), which was converted into the semicarbazone by heating its solution in alcohol (7 c.c.) at 75° for 1 hour with a solution of semicarbazide hydrochloride (3·0 g.) in a mixture of alcohol (10 c.c.) and pyridine (3 c.c.). The colourless highly insoluble semicarbazone, which rapidly separated, was collected and the free ketone, regenerated by boiling 20% hydrochloric acid (200 c.c.) under reflux (1 hour), was extracted with ether. Evaporation of the dried ethereal solution gave 4-*keto*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*-1-*carboxylic acid* (2·3 g.) as an oil, which solidified. Recrystallisation from benzene–light petroleum (b. p. 60—80°) gave the acid in slightly yellow prisms, m. p. 146·5—148·5° (Found: C, 74·7; H, 5·0. $C_{15}H_{12}O_3$ requires C, 75·0; H, 5·0%).

1 : 2 : 3 : 4-*Tetrahydrophenanthrene*-1-*carboxylic Acid*.—4-Keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-1-carboxylic (1·2 g.) was reduced as was the 1-keto-4-carboxylic acid. A mixture of 1 : 2 : 3 : 4-tetrahydrophenanthrene (0·3 g.), identified as picrate, and 1 : 2 : 3 : 4-*tetrahydrophenanthrene*-1-*carboxylic acid* (0·7 g.) was obtained. The latter compound crystallised from benzene in colourless needles, m. p. 160—162° (Found: C, 79·9; H, 6·4. $C_{15}H_{14}O_2$ requires C, 79·7; H, 6·2%). The *methyl* ester, prepared by diazomethane, crystallised from ice-cold methyl alcohol in colourless needles, m. p. 55—55·5° (Found: C, 80·2; H, 6·6. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%).

3-*Keto*-4 : 5-*benzindane*-2-β-*propionic Acid*.—A solution of α-2-naphthylmethylglutaric acid (5·0 g.) (Ansell and Hey, *loc. cit.*) in anhydrous hydrogen fluoride (100 g.) was kept for 24 hours and then poured

on ice. An oil separated which on stirring solidified, and was filtered off, washed, and dried, to give **3-*keto*-4 : 5-*benzindane*-2-β-*propionic acid*** (4·3 g.), m. p. 135—141°. Recrystallisation from benzene gave the acid, m. p. 141—142° (Found : C, 75·1; H, 5·3. $C_{14}H_{14}O_3$ requires C, 75·8; H, 5·5%).

4 : 5-*Benzindane*-2-β-*propionic Acid.*—The foregoing acid (2·0 g.), amalgamated zinc (5·0 g.), water (3·5 c.c.), hydrochloric acid (9 c.c.), glacial acetic acid (6 drops), and toluene (5 c.c.) were boiled under reflux for 24 hours, during which a further quantity of hydrochloric acid (10 c.c.) was added. The mixture was then extracted as for **1 : 2 : 3 : 4-**tetrahydro-1-naphthoic acid. Distillation of the oil obtained on evaporation of the dried extracts gave **4 : 5-*benzindane*-2-β-*propionic acid*** (1·5 g.), b. p. 196°/0·07 mm., which immediately solidified. Recrystallisation from benzene gave the acid in clusters of colourless needles, m. p. 107·5—108·5° (Found : C, 80·3; H, 6·5. $C_{14}H_{14}O_2$ requires C, 80·0; H, 6·7%).

Oxidation of* 3-*Keto*-4 : 5-*benzindane*-2-β-*propionic Acid.—**3-**Keto-**4 : 5-**benzindane-2-β-propionic acid (0·5 g.) was heated at 60—70° for 24 hours with a solution of potassium ferricyanide (30 g.) and potassium hydroxide (5·5 g.) in water (100 c.c.). When cold the solution was filtered and acidified. The precipitated acid was collected and sublimed at 180—200° under reduced pressure, to give the naphthalene-1 : 2-dicarboxylic anhydride (0·09 g.) in small needles, m. p. 164—168°. Resublimation, followed by recrystallisation from benzene–light petroleum (b. p. 60—80°), raised the m. p. of the anhydride to 167—168°. Freund and Fleischer (*Annalen*, 1913, **399**, 213) record m. p. 168—169° and Kruber (*Ber.*, 1932, **65**, 1388) records m. p. 163—164° for this anhydride.

4-*Keto*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*-3-β-*propionic Acid.*—A solution of α-(2-2′-naphthylethyl)-glutaric acid (6·0 g.) (Ansell and Hey, *loc. cit.*) in anhydrous hydrogen fluoride (100 g.) was kept for 24 hours, and then poured on ice. The precipitated solid was filtered, washed with water, and dried, to give **4-*keto*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*-3-β-*propionic acid*** (5·6 g.), m. p. 138—146°. Further recrystallisation from aqueous alcohol gave small needles (3·6 g.), m. p. 152—153° (Found : C, 76·3; H, 5·7. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%).

1 : 2 : 3 : 4-*Tetrahydrophenanthrene*-3-β-*propionic Acid.*—4-Keto-1 : 2 : 3 : 4-tetrahydrophenanthrene-3-β-propionic acid (2·7 g.) was reduced as for the 1-keto-4-carboxylic acid, with 85% hydrazine hydrate (2·0 c.c.), potassium hydroxide (1·9 g.), and diethylene glycol (15 c.c.). The reduction product was dissolved in ether, the ethereal solution extracted with 5% aqueous sodium carbonate solution, and **1 : 2 : 3 : 4-*tetrahydrophenanthrene*-3-β-*propionic acid*** (2·2 g.) precipitated by acidification of the alkaline solution. Recrystallisation from benzene–light petroleum (b. p. 60—80°) gave the acid in small needles, m. p. 157—158° (Found : C, 80·1; H, 7·1. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%).

Phenanthrene*-3-β-*propionic Acid.—A mixture of the above tetrahydro-acid (0·355 g.) and sulphur (0·09 g.) was heated at 220—250° for 2 hours. When cold the reaction mixture was digested with 5% aqueous sodium hydroxide solution (30 c.c.), treated with charcoal, and filtered. Acidification of the filtrate gave crude phenanthrene-3-β-propionic acid (0·254 g.), which after crystallisation from aqueous acetic acid, followed by 2 recrystallisations from benzene, was obtained in glistening plates, m. p. 161—163°. Bachmann and Kloetzel (*loc. cit.*) record m. p. 158·5—159·5°. The methyl ester, prepared by diazomethane, crystallised from ice-cold methyl alcohol in plates, m. p. 60—61°. Bachmann and Kloetzel (*loc. cit.*) record m. p. 63—64° for this ester.

The work described in this paper was carried out during the tenure by one of us (M. F. A.) of a University of London Post-Graduate Studentship.

KING'S COLLEGE, UNIVERSITY OF LONDON,
STRAND, LONDON, W.C.2.

[*Received, June* 17*th*, 1950.]

---

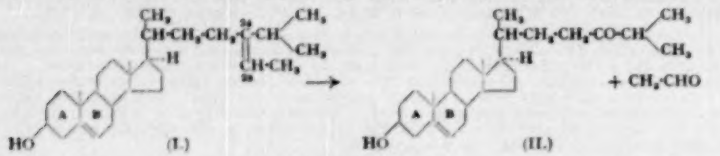
560. *The Steroid Series. Part I. The Ozonolysis of Fucosterol and Some of its Derivatives.*

By D. H. HEY, JOHN HONEYMAN, and W. J. PEAL.

The constitution and stereochemical configuration of fucosterol (I) has been confirmed by the isolation of acetaldehyde and 24-ketocholesterol (II) on ozonolysis. The 24-ketocholesterol has been converted into cholesterol by reduction. Similar ozonolyses of fucosteryl acetate, fucosteryl methyl ether, and fucostadienone are also described.

THE first evidence for the existence of a sterol in algæ was obtained by Willstätter and Page (*Annalen*, 1914, **404**, 237), who detected a new sterol in *Fucus vesiculosus*. Heilbron, Phipers, and Wright (*Nature*, 1934, **133**, 419; *J.*, 1934, 1572) isolated the pure sterol, to which they gave the name fucosterol, from this sea-weed, and its presence in many other algæ was later demonstrated by Carter, Heilbron, and Lythgoe (*Proc. Roy. Soc., B*, 1939, **128**, 82). Oxidation of fucosterol by perbenzoic acid and bromination showed the presence of two double bonds in the molecule. Further, since fucosterol was readily reduced to fucostanol, which is identical with stigmastanol, it is clear that fucosterol can differ from stigmasterol only in the positions of the double bonds. Because no volatile product was obtained on the ozonolysis of fucosterol it was considered that both of the double bonds were located in the nucleus (Heilbron, Phipers, and Wright, *loc. cit.*), but further oxidation studies to elucidate the positions occupied by the double

bonds were unsuccessful (Coffey, Heilbron, Spring, and Wright, *J.*, **1935**, 1205). The claim was made by Bengtsson (*Z. physiol. Chem.*, **1935**, **237**, 46) that fucostanol was not identical with stigmastanol, but the preparation of further derivatives confirmed their identity beyond all doubt (Coffey, Heilbron, and Spring, *J.*, **1936**, **738**; Larsen, *J. Amer. Chem. Soc.*, **1938**, **60**, 2431). One of the two double bonds of fucosterol was found to be more readily hydrogenated than the other, and in this way " α "-dihydrofucosterol was obtained and was shown to be identical with " β "-sitosterol having its double bond at the 5 : 6 position in ring B. The corresponding ketone,



" α "-fucostenone, was shown to have a conjugated system. " α "-Dihydrofucosterol thus resembles cholesterol in having a 5 : 6 double bond, which moves into the 4 : 5 position when the secondary hydroxyl group at position 3 is oxidised. The position of the second double bond in fucosterol remained in doubt until MacPhillamy (*J. Amer. Chem. Soc.*, **1942**, **64**, 1732) showed that acetaldehyde was obtained after the sterol had been treated with ozone for a much shorter time than had been used by the earlier workers (Heilbron, Phipers, and Wright, *loc. cit.*). This indicated that the second double bond is located in the side chain between carbon atoms 24 and 28, as indicated in (I).

The experiments of MacPhillamy have now been repeated and his conclusions confirmed. In one experiment when the ozonisation was deliberately restricted to ten minutes, the yield of acetaldehyde (as the dimedon derivative) corresponded to 76% of the theoretical quantity, calculated on the weight of fucosterol not recovered. After the acetaldehyde had been removed from the ozonolysis products, there remained a waxy solid or oil, the nature of which depended on the time of ozonisation. Under certain experimental conditions it has been possible to isolate from this residue pure 24-ketocholesterol (II), a compound which had already been described by Riegel and Kaye (*J. Amer. Chem. Soc.*, **1944**, **66**, 723), who prepared it by the action of cadmium diisopropyl on 3-acetoxychol-5-enyl chloride. Since the 24-ketocholesterol thus obtained has been converted into cholesterol by reduction both by Clemmensen's and by the Wolff–Kishner method (Riegel and Kaye), the complete conversion of fucosterol into cholesterol is made possible. In similar manner the ozonolysis of fucosteryl acetate gave 24-ketocholesteryl acetate, which has been hydrolysed to 24-ketocholesterol, and fucosteryl methyl ether has been converted into 24-ketocholesteryl methyl ether, and fucostadienone into 24-ketocholestenone. It was further found that if the time in the ozonisation of fucosterol was prolonged (*e.g.*, 3 hours with 4% ozone) no acetaldehyde was obtained. This probably provides the reason for the failure of Heilbron, Phipers, and Wright (*loc. cit.*) to isolate acetaldehyde in their experiments.

The isolation and identification of both the fragments resulting from the ozonolysis of fucosterol and its derivatives now place the constitution and configuration of fucosterol beyond all doubt.

Experimental.

Fucosterol.—The fucosterol used in this work was in part extracted directly from *Fucus vesiculosus* by the methods described by Heilbron, Phipers, and Wright (*loc. cit.*). Supplies of *Fucus vesiculosus* were received from Mr. A. H. Fennall, British Schering Manufacturing Laboratories Ltd., and also from Dr. J. Wilkinson of the University College of the South-West, Exeter. Extracts containing crude fucosterol were obtained from Dr. L. N. Owen, Imperial College of Science and Technology, London, S.W.7, from material supplied by the Scottish Seaweed Research Association, and also from Mr. A. H. Fennall. Samples of crude fucosterol were also supplied by Professor E. R. H. Jones. Specimens of crude fucosterol were purified by converting them into the acetate as described below. After recrystallisation the acetate was stirred into boiling methanol containing about 0·2% of sodium methoxide, and pure fucosterol crystallised on cooling. The pure sterol formed soft, feathery crystals, m. p. 124°, $[\alpha]_D^{20}$ −41·8° (*c*, 5 in chloroform). Heilbron *et al.* record m. p. 124°, $[\alpha]_D^{20}$ −38·42°, and MacPhillamy (*loc. cit.*) gives m. p. 121°, $[\alpha]_D^{20}$ −41°.

Fucosteryl Acetate.—Fucosterol (1 g.) was heated on a boiling water-bath with acetic anhydride (5 c.c.) and anhydrous sodium acetate (0·5 g.) for 1 hour. The solution was poured on ice and, after being left overnight, the crystalline product was collected. Recrystallisation from ethanol gave pure fucosteryl acetate (1 g.), m. p. 118°, $[\alpha]_D^{20}$ −45·9° (*c*, 5·1 in chloroform). MacPhillamy records m. p. 118°, $[\alpha]_D$ −45°; Heilbron, Phipers, and Wright record m. p. 118—119°, $[\alpha]_D$ −43·8° (*c*, 5 in chloroform).

Fucosteryl Toluene-p-sulphonate.—A solution of fucosterol (2 g.) and toluene-*p*-sulphonyl chloride (1·5 g.) in pyridine (5 c.c.) was kept at room temperature for 4 days. Crystallisation from acetone of the solid which separated on the addition of water gave the *toluene-p-sulphonate* (2·2 g.) in fine needles, m. p. 109—110°, $[\alpha]_D^{20}$ −38·4° (*c*, 1·0 in chloroform) (Found: C, 76·4; H, 9·4; S, 5·7. $C_{35}H_{52}O_3S$ requires C, 76·3; H, 9·4; S, 5·6%) (Coffey, Ph.D. Thesis, Univ. Manchester, 1937, records m. p. 108—109°, $[\alpha]_D^{20}$ −38·9° (*c*, 1·4 in chloroform)).

Fucosteryl Methyl Ether.—A solution of fucosteryl toluene-*p*-sulphonate (2 g.) in methanol (10 c.c.) was boiled under reflux for 1 hour. Recrystallisation from methanol of the crystalline solid which separated on cooling gave the *methyl ether* (1·4 g.), m. p. 70—71°, $[\alpha]_D^{20}$ −47·2° (*c*, 2·2 in chloroform) (Found: C, 84·4; H, 11·6; OMe, 7·2. $C_{30}H_{50}O$ requires C, 84·4; H, 11·7; OMe, 7·3%). Coffey (*loc. cit.*) records m. p. 70—71°, $[\alpha]_D^{20}$ −45·7° (*c*, 2·1 in chloroform).

Fucostadienone.—Fucosterol was oxidised to fucostadienone by the method described by Jones, Wilkinson, and Kerlogue (*J.*, 1942, 391).

Ozonolysis Experiments.—(i) Ozonised oxygen containing 4% by wt. of ozone was passed through a cooled suspension of fucosterol (1 g.) in acetic acid (25 c.c.) and then through a wash-bottle containing water (*ca.* 50 c.c.). After 20 minutes the acetic acid solution and the water were united and diluted with water to 100 c.c. This solution was fractionated through a short column and a solution of *p*-nitrophenylhydrazine (0·5 g.) in acetic acid (20 c.c.; 50%) was added to the first 20 c.c. of the distillate. Recrystallisation of the yellow crystalline precipitate several times from alcohol gave acetaldehyde *p*-nitrophenylhydrazone, m. p. 125—126°, both alone and on admixture with an authentic specimen.

(ii) Ozonolysis of fucosterol (1·25 g.) was carried out for 10 minutes under the conditions described above and a solution of dimedone (0·5 g.) in water (100 c.c.) was added to the first 20 c.c. of the distillate. Recrystallisation of the precipitate from aqueous methanol gave the acetaldehyde–dimedone compound (0·34 g.), m. p. 140—141°, both alone and on admixture with an authentic specimen. After the acetaldehyde had been distilled off from the ozonolysis products, there remained a waxy solid which was collected. Several recrystallisations from methanol gave fucosterol (0·65 g.), m. p. and mixed m. p. 124°.

(iii) Fucosterol (1 g.) was ozonised for 20 minutes as described above. The acetic acid solution so obtained was diluted to 100 c.c. with water and then boiled in an open vessel until free from acetaldeyde. The aqueous suspension was extracted with chloroform, and the chloroform solution washed with aqueous sodium carbonate and dried. Evaporation of the solvent left crude 24-ketocholesterol (0·4 g.). A solution of the latter in methanol deposited a small quantity of fucosterol, and the purified 24-ketocholesterol was obtained by adding water to the methanol solution. Recrystallisation from aqueous methanol gave pure 24-ketocholesterol, m. p. 137—138°, $[\alpha]_D^{20}$ −39° (*c*, 0·89 in chloroform) [semicarbazone, m. p. 167—168°; 2 : 4-*dinitrophenylhydrazone* (recrystallised from ethanol), m. p. 147—148° (Found: C, 68·2; H, 8·2; N, 9·5. $C_{33}H_{44}O_5N_4$ requires C, 68·3; H, 8·3; N, 9·7%)]. Riegel and Kaye (*loc. cit.*) record m. p. 137—138·5°, $[\alpha]_D^{20}$ −37° (*c*, 1 in chloroform), for 24-ketocholesterol, and m. p. 166—168° for the semicarbazone.

(iv) Fucosterol (1 g.) was ozonised for 3 hours as described above. No acetaldehyde was detected in the distillate and no insoluble material separated from the residual solution when these were treated as before.

(v) Ozone (4%) was passed for 30 minutes through a suspension of fucosteryl acetate (1 g.) in cooled glacial acetic acid (50 c.c.). By following the method described above for the isolation of 24-ketocholesterol, there was obtained 24-ketocholesteryl acetate (0·6 g.), which after recrystallisation from alcohol, had m. p. 127—128°, $[\alpha]_D^{20}$ −43° (*c*, 2·38 in chloroform). Riegel and Kaye (*loc. cit.*) record m. p. 127·5—128°, $[\alpha]_D^{20}$ −41° (*c*, 1·9 in chloroform). *24-Ketocholesteryl acetate* 2 : 4-*dinitrophenylhydrazone*, recrystallised from methanol–ethyl acetate, had m. p. 169—170° (Found: C, 67·1; H, 8·2; N, 9·4. $C_{35}H_{48}O_6N_4$ requires C, 67·5; H, 8·1; N, 9·0%). A solution of 24-ketocholesteryl acetate (0·34 g.) in methanol (25 c.c.) was mixed with methanol (25 c.c.) to which sodium (0·1 g.) had been added. The solution was boiled and then concentrated to half the volume. After addition of water (5 c.c.) and acetic acid (0·2 c.c.) the crystalline precipitate was collected. Recrystallisation from aqueous methanol gave 24-ketocholesterol (0·25 g.), m. p. and mixed m. p. 137—138°. This method for preparing 24-ketocholesterol is preferable to the direct ozonolysis of fucosterol as regards both yield and purity of product.

(vi) Fucosteryl methyl ether (0·9 g.) was ozonised under the conditions described for the acetate. The acetic acid solution was diluted with water and, after it had been boiled to remove acetaldehyde, a solid separated. Several recrystallisations from methanol gave *24-ketocholesteryl methyl ether* (0·5 g.), m. p. 129—130°, $[\alpha]_D^{20}$ −45·4° (*c*, 1·2 in chloroform) (Found: C, 81·1; H, 11·0. $C_{31}H_{44}O_2$ requires C, 81·2; H, 11·1%) [2 : 4-*dinitrophenylhydrazone*, m. p. 151—152° (Found: C, 68·5; H, 8·3; N, 9·6. $C_{44}H_{56}O_5N_4$ requires C, 68·7; H, 8·4; N, 9·6%)].

(vii) Ozone (3%) was passed for 40 minutes through a suspension of fucostadienone (1 g.) in glacial acetic acid (25 c.c.). After dilution with water and boiling to remove acetaldehyde the precipitated solid was collected. Repeated recrystallisation from methanol gave *24-ketocholestenone* (0·4 g.), m. p. 90—91° (Found: C, 81·0; H, 10·6. $C_{27}H_{42}O_2$ requires C, 81·2; H, 10·8%) [*bis*-2 : 4-*dinitrophenylhydrazone*, m. p. 228—229° (Found: C, 61·3; H, 6·6; N, 14·6. $C_{39}H_{48}O_8N_8$ requires C, 61·7; H, 6·7; N, 14·8%)].

Reduction of 24-Ketocholesterol to Cholesterol.—Concentrated hydrochloric acid (300 c.c.) was added gradually (10-c.c. portions) during 48 hours to boiling acetic acid (300 c.c.) containing 24-ketocholesterol (1 g.) and amalgamated zinc (20 g.). After cooling, the aqueous liquid was extracted with ether. After the ethereal solution had been washed free from acid with saturated aqueous sodium hydrogen carbonate and dried ($CaCl_2$), the ether was evaporated off under reduced pressure. The residual syrup was boiled with acetic anhydride (3 c.c.). On pouring of the solution on ice a syrup was obtained which, on trituration, followed by recrystallisation from methanol, gave cholesteryl acetate (0·1 g.), m. p. and mixed m. p. with an authentic specimen 113—114°, $[\alpha]_D^{20}$ −45° (*c*, 0·6 in chloroform). Deacetylation

with sodium in methanol, followed by recrystallisation from methanol, gave cholesterol, m. p. and mixed m. p. with an authentic specimen 149—150°. When 24-ketocholesterol (0·5 g.) was reduced by the Wolff–Kishner method under the conditions described by Riegel and Kaye (*loc. cit.*) there was obtained cholesterol (0·15 g.), m. p. and mixed m. p. with an authentic specimen 147—149°.

The authors thank Mr. A. H. Fennall, Professor E. R. H. Jones, F.R.S., Dr. L. N. Owen, Dr. J. Wilkinson, the Scottish Seaweed Research Association and British Schering Manufacturing Laboratories Ltd. for assistance with the raw materials required for this work.

KING'S COLLEGE, UNIVERSITY OF LONDON,
STRAND, LONDON, W.C.2. [*Received, July 13th*, 1950.]

---

561. *The Structure of the Starch-type Polysaccharide Synthesised from Sucrose by* Neisseria perflava.

By S. A. BARKER, E. J. BOURNE, and M. STACEY.

The polysaccharide synthesised from sucrose by cultures of *Neisseria perflava* (strain II—1) has properties intermediate between those of amylopectin and glycogen, approximating more closely to those of the latter. Its average chain length is 11—12 glucose units.

IN 1946 Hehre and Hamilton (*J. Biol. Chem.*, 1946, **166**, 777) reported that *Neisseria perflava*, a Gram-negative coccus inhabiting the throats of healthy people, synthesises from sucrose, and to a smaller extent from glucose-1 phosphate, a polysaccharide of the amylopectin–glycogen class. It was shown subsequently that the washed cells of this organism (Hehre and Hamilton, *J. Bact.*, 1948, **55**, 197) and a cell-free enzyme system derived therefrom (Hehre, Hamilton, and Carlson, *J. Biol. Chem.*, 1949, **177**, 267) also catalyse the formation of an iodine-staining polysaccharide from these substrates. The American workers furnished strong evidence that *Neisseria perflava* utilises two enzymes, a phosphorylase and an amylosucrase, for the synthesis of 1 : 4-linked chains of α-D-glucose units.

Hehre, Hamilton, and Carlson (*loc. cit.*) observed that whereas the polysaccharide produced by growing cultures is similar to maize amylopectin, that synthesised by the cell-free enzyme system more closely resembles glycogen. Dr. E. J. Hehre of the Cornell Medical School, New York, drew our attention to this fact and, at his suggestion, we have examined a polysaccharide isolated by him from *Neisseria perflava* cultures of a different strain (II—1) from that employed in the work mentioned above (19—34).

The bacterial polysaccharide was obtained free from proteins and other nitrogenous compounds and had an ash content of 1·3%. It dissolved slowly in cold water and rapidly in hot water to give an opalescent solution, which was stained reddish-purple with small amounts of iodine and red with larger amounts. Its reducing power, as measured by cuprimetric titration, was only 0·1% of that of glucose. The polysaccharide was not stained at 105° by ammoniacal silver nitrate or by an acid solution of resorcinol, and thus was virtually free from reducing aldoses and ketoses and also from acid-labile ketose sugars such as sucrose. Chromatographic analysis of a hydrolysate, obtained by heating the polysaccharide at 100° for 5 hours with 2N-sulphuric acid, revealed a single aldose component; this had an R_y value identical with that of glucose. Since no ketose was detected, the polysaccharide contained none of the fructose moiety of the sucrose substrate. The reducing power of such a hydrolysate corresponded to a 93—94% conversion into glucose.

Treatment of an aqueous solution of the bacterial polysaccharide with thymol under conditions which are favourable for the fractionation of potato and other starches (Bourne, Donnison, Haworth, and Peat, *J.*, 1948, 1687) did not afford an insoluble complex. The blue value of the polysaccharide (0·09) was closely related to that of waxy maize starch (0·10; Bourne and Peat, *J.*, 1949, 5); it was intermediate between the blue values of guinea-pig liver glycogen (0·01) and of the purest samples of potato amylopectin prepared in these laboratories (0·14—0·18). Clearly the bacterial polysaccharide could have contained no more than a trace of amylose (B.V., 1·2—1·4). It will be recalled that Hehre, Hamilton, and Carlson (*loc. cit.*) showed that the polysaccharide synthesised by cultures of the 19—34 strain of *Neisseria perflava* likewise had a blue value intermediate between the blue values of glycogen and amylopectin and gave no precipitate when treated in aqueous solution with "Pentosol" (a commercial mixture of primary amyl alcohols) or butanol.

More detailed information regarding the structure of the bacterial polysaccharide (strain II—1) was obtained (*a*) by β-amylolysis, and (*b*) by methylation and end-group assay. The

limiting conversion into maltose with soya-bean β-amylase was 55—59% [cf. 57—59% for the polysaccharide from cultures of the 19—34 strain (Hehre, Hamilton, and Carlson, *loc. cit.*)]; the same enzyme sample was known to give 56% maltose from potato amylopectin (B.V., 0·21). Glycogens are usually regarded as having a somewhat lower conversion limit than this (Hopkins, Cope, and Green, *J. Inst. Brewing*, 1933, **39**, 487; Morris, *J. Biol. Chem.*, 1944, **154**, 503; Jeanloz, *Helv. Chim. Acta*, 1944, **27**, 1501; Hehre, Hamilton, and Carlson, *loc. cit.*), but Meyer and Jeanloz (*Helv. Chim. Acta*, 1943, **26**, 1784) have suggested that a low conversion may sometimes be caused by the inability of β-amylase to penetrate the more complex regions of the highly-branched glycogen structure. The limit dextrin produced by β-amylolysis of the bacterial polysaccharide, like that prepared from glycogen by Meyer and Fuld (*Helv. Chim. Acta*, 1941, **24**, 375), was stained faintly brown by iodine, in contrast to the relatively intense reddish-purple stain given by the limit dextrin derived from potato amylopectin. The blue value of the bacterial dextrin was *ca.* 0·01, whereas the potato dextrin has B.V., 0·15—0·20 (Bourne, Haworth, Macey, and Peat, *J.*, 1948, 924; Bourne, Stitch, and Peat, *J.*, 1949, 1448).

A hydrolysate of the methylated bacterial polysaccharide (OMe, 45·1%) gave, on a filter paper chromatogram, three spots, having R_F values identical with those of 2 : 3-dimethyl, 2 : 3 : 6-trimethyl, and 2 : 3 : 4 : 6-tetramethyl glucose. A quantitative assay on filter paper, with a technique which was essentially that described by Hirst, Hough, and Jones (*J.*, 1949, 928), showed the average chain length of the polysaccharide ether to be 11—12 glucose units, a value which agrees closely with the reported chain lengths of most glycogens (cf. Halsall, Hirst, and Jones, *J.*, 1947, 1399). The same method gave an average chain length of 20—21 glucose units for methylated potato amylopectin (Barker, Bourne, and Wilkinson, *J.*, 1950, in the press).

Thus the polysaccharides synthesised from sucrose by cultures of the 19—34 and the II—1 strain of *Neisseria perflava* appear to be closely related; they have properties intermediate between those usually accepted for glycogen and amylopectin. The balance of the above evidence tends to favour a glycogen structure for the latter bacterial polysaccharide, but we are of the opinion that there is no clear-cut distinction in nature between glycogen and amylopectin, since these two polysaccharides are synthesised by closely similar processes (Cori, Swanson, and Cori, *Fed. Proc.*, 1945, **4**, 234; Barker, Bourne, Wilkinson, and Peat, *J.*, 1950, **93**). It is already known, for example, that some samples of rabbit liver glycogen have an average chain length of 18 glucose units (Haworth, Hirst, and Isherwood, *J.*, 1937, 577; Halsall, Hirst, and Jones, *loc. cit.*) and that a fraction of the polysaccharide from the Golden Bantam variety of sweet corn has an average chain length of 11 glucose units (Dvonch and Whistler, *J. Biol. Chem.*, 1949, **181**, 889). The different properties reported by Hehre and his colleagues (see above) for the polysaccharides synthesised by *Neisseria perflava* cultures and by the cell-free enzyme system may well have been caused by the preferential separation or even destruction, during the rupturing of the cells, of the enzymes responsible for the synthesis of 1 : 4-links relative to those which catalyse the formation of 1 : 6-links.

Experimental.

Isolation of the Bacterial Polysaccharide.—The polysaccharide (2·5 g.) was kindly provided by Dr. E. J. Hehre, by whom it had been isolated from the fluids of a sucrose-broth culture of *Neisseria perflava* (strain II—1); it had $[\alpha]_D^{17}$ +178° (*c*, 0·1 in 0·5*N*-sodium hydroxide). The method of preparation was similar to that employed by Hehre, Hamilton, and Carlson (*loc. cit.*) for the isolation of the polysaccharide synthesised by the 19—34 strain of *Neisseria perflava*.

Purity of the Polysaccharide.—(a) *Ash content.* Heated to constant weight in a micro-muffle furnace, the polysaccharide gave 1·5% of ash.

(b) *Nitrogenous impurities.* Negative reactions were obtained when the polysaccharide was tested for nitrogenous impurities by fusion with sodium, and for proteins by treatment with Millon's mercuric nitrite reagent.

(c) *Reducing sugars.* The reducing power of a solution (5 c.c.), containing the polysaccharide (30·6 mg.) and glucose (0·50 mg.), was measured by means of the Shaffer–Hartmann copper reagent (*J. Biol. Chem.*, 1921, **45**, 377), calibrated against glucose. The reducing power of the polysaccharide, calculated by difference, was 0·1%, in terms of glucose.

Spots of a solution (2%) of the polysaccharide, applied to filter papers, were sprayed (i) with an ammoniacal solution of silver nitrate, and (ii) with an acid solution of resorcinol. Neither reagent gave a stain when heated to 105°, showing the virtual absence of reducing sugars of both the aldose and the ketose series, and of acid-labile sugars, such as sucrose, which yield a ketose on hydrolysis.

(d) *Reducing sugars liberated during acidic hydrolysis.* (i) The polysaccharide (40 mg.) was heated at 100° for 5 hours with 2*N*-sulphuric acid (1 c.c.) in a sealed tube. The hydrolysate and water washings (1 c.c.) were neutralised with barium carbonate and centrifuged. Spots of the supernatant solution and of three reference solutions (2%), containing glucose, fructose, and sucrose, respectively, were applied to a sheet of filter paper (Whatman No. 1) and irrigated for 24 hours with aqueous butanol, as described by

Partridge (*Nature*, 1946, **158**, 270). After drying, the sheet was developed with ammoniacal silver nitrate. The reference solutions of glucose and fructose and the hydrolysate of the polysaccharide each gave one spot, the R_F value of the unknown sugar being indistinguishable from that of glucose. A similar sheet, developed with acid resorcinol, revealed the reference fructose and sucrose spots, but no spot from the hydrolysate of the polysaccharide.

(ii) Duplicate samples (*ca.* 25 mg.) of the dry polysaccharide were hydrolysed for 5 hours with 7% sulphuric acid and analysed by cuprimetric titration, as described by Bourne, Donnison, Haworth, and Peat (*loc. cit.*). The reducing powers of the neutral hydrolysates corresponded to conversions into glucose of 93 and 94%, respectively.

Treatment of the Polysaccharide with Thymol.—Powdered thymol (0·2 g.) was added to an aqueous solution (30 c.c.) of the bacterial polysaccharide, and the suspension was kept at 30° for 3 days. No insoluble polysaccharide–thymol complex was formed.

Iodine Stain.—The polysaccharide was stained with iodine under the standard conditions for the determination of blue value (B.V.) described by Bourne, Haworth, Macey, and Peat (*loc. cit.*). The final solution contained the polysaccharide (1 mg./100 c.c.), iodine (2 mg./100 c.c.), and potassium iodide (20 mg./100 c.c.). The absorption values (A.V.) of this solution are compared in the following table with those obtained when samples of potato amylopectin, prepared by the *cyclo*hexanol method (Bourne, Donnison, Haworth, and Peat, *loc. cit.*), and glycogen from guinea-pig liver are stained under similar conditions.

TABLE I.

Absorption values of polysaccharide–iodine solutions.

	A.V. at λ:							
Polysaccharide.	4300 A.	4700 A.	4900 A.	5200 A.	5500 A.	5800 A.	6000 A.	6800 A.
Potato amylopectin *	0·45	0·34	0·30	0·29	0·30	0·28	0·25	0·18
Neisseria perflava polysaccharide	0·52	0·37	0·34	0·31	0·26	0·21	0·13	0·09
Glycogen from guinea-pig liver †	0·38	0·21	0·14	0·08	0·04	0·02	0·01	0·01

* From a graph given by Bourne, Donnison, Haworth, and Peat (*loc. cit.*).
† Kindly supplied by Dr. F. Smith.

Treatment of the Polysaccharide with β-Amylase.—(a) *Conversion limit.* The bacterial polysaccharide was submitted to β-amylolysis under the conditions described by Bourne, Donnison, Haworth, and Peat (*loc. cit.*). The percentage conversion into maltose was 42 (30 minutes), 54 (180 minutes), and 55 (270 minutes).

(b) *Isolation of the limit dextrin.* A solution of the polysaccharide (260·9 mg.) in 0·5*N*-sodium hydroxide (20 c.c.) was neutralised with sulphuric acid and buffered at pH 4·7 with *M*-acetate buffer (pH, 7·0; 10 c.c.) and *N*-acetic acid (10 c.c.). After the addition of a 0·2% solution (30 c.c.) of soya-bean β-amylase (Bourne, Macey, and Peat, *J.*, 1945, 882), the solution was diluted with water to 100 c.c. and incubated at 28°. Estimations of reducing power by the Shaffer–Hartmann method (*loc. cit.*) indicated that the conversion limit was reached after 18 hours. Three hours later, the digest was inactivated by immersion in a boiling water-bath and the coagulated protein was removed by filtration. The reducing power of the filtrate corresponded to a 59% conversion into maltose. The solution was dialysed in Cellophane against frequent changes of distilled water for 3 days and then freeze-dried. The limit dextrin (75·5 mg.) represented 30% of the original polysaccharide (allowance being made for the digest samples which had been removed for analytical purposes).

The limit dextrin gave a brown iodine stain in high concentration, but gave no detectable stain under the conditions required for the determination of blue value (see above). A solution containing the dextrin (5 mg./100 c.c.), iodine (2 mg./100 c.c.), and potassium iodide (20 mg./100 c.c.) had the absorption values quoted in Table II.

TABLE II.

Absorption values of the dextrin–iodine solution.

	A.V. at λ:							
Solution.	4300 A.	4700 A.	4900 A.	5200 A.	5500 A.	5800 A.	6000 A.	6800 A.
Dextrin + I_2 + KI	0·43	0·27	0·21	0·14	0·11	0·07	0·03	0·02
I_2 + KI	0·35	0·19	0·11	0·06	0·03	0·02	0·01	0·01

Methylation of the Bacterial Polysaccharide.—The bacterial polysaccharide (0·963 g.) was methylated with sodium and methyl iodide in liquid-ammonia suspension at −70° (Freudenberg and Boppel, *Ber.*, 1938, **71**, 2505). In all 15 alternate additions of sodium and methyl iodide were made. The liquid ammonia was allowed to evaporate at room temperature, the final traces being removed at 100°/12 mm. The residue was dissolved in water and dialysed for three days against frequent changes of distilled water. The solution was concentrated by freeze-drying to a white solid, which was finally dried at 60° over phosphoric oxide in a vacuum. The methylated polysaccharide (0·808 g.) had OMe, 45·1% (the trimethyl ether of a polyglucose requires OMe, 45·6%).

Identification of the Methyl Sugars Obtained from the Methylated Polysaccharide.—The methylated polysaccharide (60 mg.) was heated for 9 hours with methanolic hydrogen chloride (3·6%, w/w; 1·2 c.c.) in a sealed tube immersed in a boiling water-bath. When cool, the tube was opened, 4% hydrochloric acid (6 c.c.) was added, and the glucoside mixture was hydrolysed at 100° for 5 hours. The mixed methyl

sugars were isolated by the method of Hirst, Hough, and Jones (*loc. cit.*) and redissolved in water (1 c.c.). In a similar manner, a hydrolysate was prepared from methylated potato amylopectin (OMe, 44·5%). A reference solution (3 c.c.), containing 2 : 3-dimethyl glucose (3·12 mg.), 2 : 3 : 6-trimethyl glucose (66·6 mg.), and 2 : 3 : 4 : 6-tetramethyl glucose (3·54 mg.), was also prepared.

Spots of the hydrolysates and of the reference solution were placed on filter paper (Whatman No. 1) and irrigated for 18 hours with a butanol solvent, as described by Hirst, Hough, and Jones (*loc. cit.*). An aniline hydrogen phthalate spray (Partridge, *Nature*, 1949, **164**, 443) revealed three spots, identical in each case.

End-Group Assay of the Methylated Polysaccharide.—The components of a hydrolysate of the methylated polysaccharide were separated by filter paper chromatography, eluted, and estimated by the hypoiodite method according to the procedure of Hirst, Hough, and Jones (*loc. cit.*) with minor modifications described by Barker, Bourne, and Wilkinson (*loc. cit.*). The results of five independent assays are shown in Table III.

TABLE III.

End-group assay of the methylated bacterial polysaccharide.

Assay number.	Molecular ratio (%) of components.		
	2 : 3-Dimethyl glucose.	2 : 3 : 6-Trimethyl glucose.	2 : 3 : 4 : 6-Tetramethyl glucose.
I	6·5	83·7	9·8
II	4·5	86·2	9·3
III	6·0	85·5	8·9
IV	5·8	85·8	8·3
V	7·4	85·1	7·4
Average	6·0	85·3	8·7

This proportion of tetramethyl glucose corresponded to a chain length of 11—12 glucose units.

The authors are indebted to Dr. E. J. Hehre for supplying the bacterial polysaccharide used in this work, to Dr. F. Smith for providing a sample of guinea-pig liver glycogen, and to the Brewing Industry Research Foundation for a grant to one of them (S. A. B.).

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, July 11th*, 1950.]

---

562. *The Synthesis of Neurotropic and Musculotropic Stimulators and Inhibitors. Part IV. Benzilic Acid Derivatives.*

By A. L. MORRISON, (MISS) M. KÖNIGSTEIN, and A. COHEN.

In view of their structural relation to both " Trasentin " and " Benadryl," 2-dialkylaminoalkyl α-(2-dialkylaminoethoxy)-αα-diphenylacetates (IV) were prepared. Some of them possess valuable spasmolytic properties.

Treatment of sodium α-(2-dimethylaminoethoxy)-αα-diphenylacetate with thionyl chloride gave 3-keto-4-methyl-2 : 2-diphenylmorpholine.

IN 1945, Loew, Kaiser, and Moore (*J. Pharm. Exp. Ther.*, 1945, **83**, 120) reported that 1-(2-dimethylaminoethoxy)-1 : 1-diphenylmethane (I; " Benadryl ") possessed pronounced histaminolytic properties. We had previously observed that allyl 1-methyl-4-phenylpiperidine-4-carboxylate was a more powerful histaminolytic than the corresponding ethyl ester (pethidine) and we therefore considered that allyl α-(2-dimethylaminoethoxy)-αα-diphenylacetate (II;

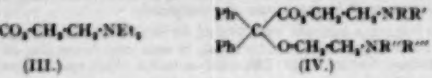
$$Ph_2CH{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}NMe_2 \quad (I.)$$

$$Ph_2C(CO_2R){\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}NR'R'' \quad (II.)$$

R = allyl, R′ = R″ = Me) might be a generally valuable spasmolytic. We also visualised that if in (II; R = allyl) the allyl radical were replaced by a 2-diethylaminoethyl radical, the resulting compound (IV; R = R′ = Et; R″ = R‴ = Me) would contain features of both " Benadryl " and the well-established neurotropic spasmolytic " Trasentin " (III). Alkyl esters of α-(2-dialkylaminoethoxy)-αα-diphenylacetic acid and -α-phenylacetic acid were readily obtained by condensing the sodio-derivatives of alkyl benzilates and alkyl mandelates with dialkyl-2-chloroethylamines. Not until 1946 (*Chem. Abstr.*, 1946, **40**, 1175) did we learn that CIBA had already prepared such esters by an identical method (B.P. 558,653; U.S.P. 2,387,447). The preparation of new esters is given in the Experimental section.

The first method employed to prepare the dibasic esters (IV) was to hydrolyse the alkyl esters (II; R′ = Et) with sodium hydroxide and condense the conveniently isolated sodium salt of the

acid with dialkyl-2-chloroethylamines, as described in the Experimental part. Later it was found that the dibasic esters were even more readily prepared from the corresponding ethyl



(III.) (IV.) (V.)

esters by transesterification using the basic alcohol in presence of a small amount of its sodium derivative. A number of dibasic esters were made by this general method and their properties are given in the table.

It was also of interest to prepare the ketone (V), as its structural similarity to amidone indicated that it might possess both spasmolytic and analgesic properties.

The preparation of 1-(2-diethylaminoethoxy)-1 : 1-diphenylbutan-2-one is described in B.P. 558,653, but as we failed to repeat this experiment, it was decided to attempt the preparation of (V) by the action of ethylmagnesium halide on the piperidide of α-(2-dimethylaminoethoxy)-αα-diphenylacetic acid. Treatment of the sodium salt of this acid with thionyl chloride (cf. G.P. 262,883) and reaction of the resultant crude product with piperidine gave only a non-basic product. The action of thionyl chloride was more closely investigated and it was found that the neutral product, m. p. 97—98°, was formed in 75% yield, and from analysis and properties was undoubtedly 3-keto-4-methyl-2 : 2-diphenylmorpholine. This reaction is analogous to those described by Tiffeneau and Führer (*Bull. Soc. chim.*, 1914, **15**, 168), wherein certain acid chlorides and bromides react with certain tertiary bases to give disubstituted amides and alkyl halides. More recently it has been reported that attempts to make the acid chloride by treatment of γ-dimethylamino-αα-diphenylvaleric acid with thionyl chloride yielded 1 : 5-dimethyl-3 : 3-diphenylpyrrolid-2-one (Gardner, Easton, and Stevens, *J. Amer. Chem. Soc.*, 1948, **70**, 2906). It is interesting to note that whereas γ-diethylamino-αα-diphenylbutyric acid is readily converted by the action of thionyl chloride into 1-ethyl-3 : 3-diphenylpyrrolid-2-one, δ-diethylamino-αα-diphenylvaleric acid does not give the 2-piperidone on similar treatment but simply the acid chloride (Dupré, Elks, Hems, Speyer, and Evans, *J.*, 1949, 500). α-(2-Dimethylaminoethoxy)-αα-diphenylacetopiperidide and the corresponding 2-diethylaminoethylamide were finally prepared from ethyl α-(2-dimethylaminoethoxy)-αα-diphenylacetate by Bodroux's method (*Compt. rend.*, 1904, **138**, 1427). All attempts to prepare a ketone by treating the piperidide with ethylmagnesium iodide were unsuccessful, the starting material being recovered (cf. Burton, *J.*, 1930, 2400).

The results of pharmacological testing of the above compounds will be reported elsewhere (Forbes and Marshall, *Brit. J. Pharmacol.*, in the press). Preliminary clinical results indicate that 2-diethylaminoethyl α-(2-dimethylaminoethoxy)-αα-diphenylacetate (Ro 3—0131) may possess valuable spasmolytic properties (Norman and Wrigley, *Acta Allerg.*, 1948, **1**, 382).

Experimental.

Allyl Mandelate.—A solution of mandelic acid (20 g.) and concentrated sulphuric acid (2 ml.) in allyl alcohol (100 ml.) was heated on the steam-bath for 16 hours. The excess of allyl alcohol was then distilled off *in vacuo* and the residue made alkaline with ice-cold sodium carbonate solution. The *ester* was extracted with ether and distilled, having b. p. 152—154°/12 mm. The oil crystallised on storage and then had m. p. 30—32° (yield, 17 g.) (Found: C, 68·0; H, 6·5%; I.V., 125·6. $C_{11}H_{12}O_3$ requires C, 68·75; H, 6·25%; I.V., 131).

Allyl Benzilate.—Benzilic acid (20 g.) was esterified with allyl alcohol as described above and the *ester* obtained as an oil, b. p. 158—160°/0·8 mm. (Found: C, 76·3; H, 6·3. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%).

Allyl α-(2-Dimethylaminoethoxy)-α-phenylacetate.—Allyl mandelate (10 g.) was added to powdered sodium (1·2 g.) in dry toluene (80 ml.), and when the sodium had reacted 2-chloroethyldimethylamine (8 g.) was added and the solution heated under reflux for 3 hours. When the reaction mixture was worked up for basic material, the *ester* was obtained as an oil, b. p. 128—130°/0·1 mm. (Found: C, 68·1; H, 8·3; N, 5·1. $C_{15}H_{21}O_3N$ requires C, 68·4; H, 8·0; N, 5·3%).

Allyl α-(2-Dimethylaminoethoxy)-αα-diphenylacetate.—This *ester*, prepared in a similar way from allyl benzilate, was obtained as an oil, b. p. 175—178°/0·05 mm. (Found: C, 73·8; H, 7·5; N, 4·7. $C_{21}H_{25}O_3N$ requires C, 74·1; H, 7·4; N, 4·1%).

Ethyl α-(2-Dimethylaminoethoxy)-αα-diphenylacetate.—To powdered sodium (11·5 g.) in toluene (550 ml.) was added gradually with cooling and stirring ethyl benzilate (128 g.) in toluene (150 ml.). When all the sodium had dissolved a dried solution of 2-chloroethyldimethylamine, liberated from the hydrochloride (85 g.), in toluene (150 ml.) was slowly added and the solution heated under reflux for 5 hours. The cooled toluene solution was then exhaustively extracted with 2N-hydrochloric acid (six times), the acid extract washed with ether and made alkaline with sodium hydroxide solution, and the

precipitated base taken up in ether. The ethereal solution, after being washed with water and dried (Na_2SO_4), was concentrated and the residual oil distilled to give the *ester*, b. p. 165—167°/0·3 mm. (120 g., 73·5%) (Found : N, 4·3. $C_{20}H_{23}O_3N$ requires N, 4·3%).

Sodium α-(2-*Dimethylaminoethoxy*)-αα-*diphenylacetate*.—Sodium (4·6 g.) was dissolved in ethanol (174 ml.), and the above ester (43·5 g.) in ethanol (174 ml.), and water (8·5 ml.), added. When the solution was heated, the *sodium* salt started to separate. Heating was continued for 1 hour, the mixture cooled in ice and filtered, and the sodium salt washed first with ice-cold alcohol and then with dry ether. It melted at 303—304° (decomp.) (35·5 g., 83·1%) (Found : Na, 7·2. $C_{18}H_{20}O_3NNa$ requires Na, 7·2%).

α-(2-*Dimethylaminoethoxy*)-αα-*diphenylacetic Acid Hydrochloride*.—The above sodium salt (1 g.) dissolved when its suspension in water was made acid with concentrated hydrochloric acid, and a crystalline product separated, which, after cooling, was filtered off and washed with dry acetone. The *hydrochloride* (0·8 g.) melted at 112—114° (Found : Cl, 10·7; N, 3·9. $C_{18}H_{22}O_3NCl$ requires Cl, 10·6; N, 4·1%).

2-*Diethylaminoethyl* α-(2-*Dimethylaminoethoxy*)-αα-*diphenylacetate*.—(*a*) To a stirred suspension of the above sodium salt (26·6 g.) in toluene (150 ml.) was added a dried solution of 2-chloroethyldiethylamine, liberated from the hydrochloride (21·6 g.), in toluene (50 ml.), and the mixture refluxed gently with stirring for 2½ hours. The sodium chloride (5·0 g.; theor., 4·9 g.) was filtered off, and the toluene solution exhaustively extracted with 2*N*-hydrochloric acid. The base was precipitated by addition of excess of 2*N*-sodium hydroxide solution and taken up in ether, and the ethereal solution washed five times with water. After being dried, the ethereal solution was concentrated and the residual oil distilled, to give the *ester*, b. p. 170°/0·05 mm., n_D^{24} 1·5290 (24·7 g., 75%) (Found : C, 72·1; H, 8·7; N, 7·1. $C_{24}H_{33}O_3N_2$ requires C, 72·3; H, 8·55; N, 7·0%).

(*b*) To dry 2-diethylaminoethanol (5·35 g.) and dry toluene (20 ml.) in a flask fitted with a short fractionating column and a ratio still head, was added sodium (0·05 g.), and the solution was heated until it refluxed (b. p. 110°). Ethyl 1-(2-dimethylaminoethoxy)-1 : 1-diphenylacetate (10 g.) in toluene (20 ml.) was then added slowly, the vapour temperature falling to 80°. Toluene and alcohol were then distilled off until all the ester had been added and the vapour temperature had risen to 110°. The toluene solution was then worked up as described in (*a*) to give 9·6 g. (79%) of product, b. p. 178°/0·1 mm., n_D^{20} 1·5282 (Found : C, 72·8; H, 8·6; N, 7·2%). The esters recorded in the Table were prepared in the same way.

Ethyl α-(2-*Morpholinoethoxy*)-αα-*diphenylacetate*.—To powdered sodium (1·8 g.) in toluene (80 ml.) at room temperature was added slowly with stirring ethyl benzilate (20 g.) in toluene (25 ml.). When all the sodium had reacted 1-2′-chloroethylmorpholine (16 g.) in toluene (25 ml.) was added and the reaction mixture refluxed for 4 hours. When worked up as described above the *ester* was obtained as an oil, b. p. 166—167°/0·1 mm. (18·6 g.) (Found : C, 71·4; H, 7·5; N, 4·5. $C_{26}H_{27}O_4N$ requires C, 71·55; H, 7·3; N, 3·8%).

Sodium α-(2-*Morpholinoethoxy*)-αα-*diphenylacetate*.—Hydrolysis of the above ester (16 g.) with alcoholic sodium hydroxide gave the *sodium* salt, m. p. 273—274° (decomp.) (14 g.) (Found : N, 3·9; Na, 6·3. $C_{20}H_{22}O_4NNa$ requires N, 3·9; Na, 6·3%).

Esters, $Ph_2C(CO_2R)\cdot O\cdot CH_2\cdot CH_2\cdot NMe_2$, *etc.*

R =	B. p., at mm.	Yield, %	Formula.	Required, %. C.	H.	N.	Found, %. C.	H.	N.
$CH_2\cdot CH_2\cdot NMe_2$	168—170° 0·2 mm.	—	$C_{22}H_{29}O_3N$	71·35	8·1	7·5	72·3	8·2	7·1
$CH_2\cdot CH_2\cdot N<([CH_2]_5)>O$	194—196° 0·1 mm.	75	$C_{23}H_{31}O_3N$	73·2	8·3	6·8	72·8	8·3	7·2
$CH_2\cdot CH_2\cdot N<^{Me}_{CH_2\cdot CH:CH_2}$	184—186° 0·1 mm.	60·8	$C_{22}H_{27}O_3N$	72·7	8·1	7·1	73·4	8·3	7·1
$CH_2\cdot CH_2\cdot N(CH_2\cdot CH:CH_2)_2$	150° 0·05 mm.	64	$C_{24}H_{31}O_3N$	73·9	8·05	6·6	73·3	8·45	6·5
$CH_2\cdot CH_2\cdot N<([CH_2]_4)>O$	192—194° 0·1 mm.	56	$C_{22}H_{29}O_4N$	—	—	6·8	—	—	6·75
$CH_2\cdot CH_2\cdot NMePr^i$	166—170° 0·2 mm.	67	$C_{24}H_{31}O_3N$	—	—	7·1	—	—	6·7
$CHMe\cdot CH_2\cdot NMe_2$	182—184° 0·1 mm.	88	$C_{23}H_{31}O_3N$	—	—	6·8	—	—	6·8
$CH_2\cdot CH_2\cdot NEt_2$ *	180—184° 0·05 mm.	80	$C_{24}H_{31}O_3N$	73·2	8·9	6·6	73·3	9·3	6·3

* $NMePr^i$ replaces NMe_2 in the general formula.

2-*Diethylaminoethyl* α-(2-*Morpholinoethoxy*)-αα-*diphenylacetate*.—Condensation of the above sodium salt (7 g.) with 2-chloroethyldiethylamine (2·9 g.) by heating them in boiling toluene (50 ml.) for 4 hours gave the basic *ester* as an oil, b. p. 200°/0·4 mm. (7·0 g.) (Found : C, 71·0; H, 8·05; N, 6·45. $C_{26}H_{34}O_4N_2$ requires C, 70·9; H, 8·2; N, 6·4%).

2-*Morpholinoethyl* α-(2-*Morpholinoethoxy*)-αα-*diphenylacetate*.—In a similar way the sodium salt (7·0 g.) on condensation with 2-chloroethylmorpholine (4 g.) gave the basic *ester*, b. p. 225—230°/0·1 mm. (6·2 g.) (Found : C, 68·8; H, 7·4; N, 6·4. $C_{26}H_{34}O_5N_2$ requires C, 68·7; H, 7·5; N, 6·2%).

Ethyl α-(2-*N*-*Methyl*-*N*-*isopropylaminoethoxy*)-αα-*diphenylacetate*.—2-*N*-Methyl-*N*-*iso*propylaminoethanol was prepared by methylation of 2-isopropylaminoethanol with formaldehyde and formic acid (cf. Clarke, Gillespie, and Weisshaus, *J. Amer. Chem. Soc.*, 1933, **55**, 4571). A fraction, b. p. 68—76°/15 mm.,

of the product was analysed (Found: N, 12·2. Calc. for $C_9H_{11}ON$: N, 11·9%). This impure product (40 g.) in chloroform (80 ml.) was treated with thionyl chloride (37 ml.) in chloroform (70 ml.) and left at room temperature overnight. The chloroform and excess of thionyl chloride were distilled off, and alcohol (30 ml.) was added. On addition of dry ether a sticky solid separated, which, even after recrystallisation from alcohol–ether, was very hygroscopic and not suitable for analysis. The crude hydrochloride (31 g.) was therefore used for the next stage of the synthesis. Ethyl benzilate (46·4 g.) was treated with sodium (4·16 g.) in toluene (100 ml.); 2-chloroethylmethyl*iso*propylamine, prepared from the hydrochloride (31 g.), was added and the mixture heated for 7 hours under reflux. Worked up in the described manner, the *ester* was obtained as an oil, b. p. 176—180°/0·2 mm. (Found: N, 4·2. $C_{23}H_{31}O_3N$ requires N, 3·9%).

3-Keto-4-methyl-2:2-diphenylmorpholine.—Sodium 1-(2-dimethylaminoethoxy)-1:1-diphenylacetate (10 g.) was added in small portions to thionyl chloride (20 ml.), and the mixture heated under reflux for 1 hour. It was then poured on ice, whereupon an oil separated and crystallised after some time. It was filtered off and dried *in vacuo* over phosphoric oxide. Recrystallised from *cyclo*hexane it gave the pure *ketomorpholine*, m. p. 97—98° (7·2 g.) (Found: C, 77·6; H, 6·2; N, 5·2. $C_{17}H_{17}O_2N$ requires C, 76·7; H, 6·3; N, 5·2%).

α-(2-Dimethylaminoethoxy)-α-diphenylacetopiperidide.—To a solution of methylmagnesium iodide, prepared from magnesium (1·2 g.) and methyl iodide (7·1 g.), in benzene (30 ml.), was added dry piperidine (4·25 g.) in benzene (20 ml.), and the mixture stirred for 30 minutes. Ethyl 1-(2-dimethylaminoethoxy)-1:1-diphenylacetate (8·1 g.) in benzene (20 ml.) was then added and the mixture heated under reflux for 1 hour with stirring. To the ice-cooled reaction mixture N-hydrochloric acid (100 ml.) was added. The aqueous layer was made alkaline with sodium hydroxide solution, and sufficient ammonium chloride added to dissolve the magnesium hydroxide. The base was extracted with ether and gave, on distillation, the pure *piperidide*, b. p. 195—206°/0·5 mm., which, recrystallised from light petroleum (b. p. 60—80°), had m. p. 94—96° (4·8 g.) (Found: C, 75·4; H, 8·2; N, 7·6. $C_{23}H_{30}O_2N_2$ requires C, 74·7; H, 8·1; N, 7·2%). The corresponding *2-diethylaminoethylamide* was prepared in the same way from *NN*-diethylethylenediamine and was obtained as an oil, b. p. 195—197°/0·5 mm. (Found: C, 72·8; H, 8·8; N, 10·5. $C_{24}H_{34}O_2N_2$ requires C, 72·5; H, 8·8; N, 10·6%).

Research Department, Roche Products Limited,
Welwyn Garden City, Herts.

[*Received, July 13th*, 1950.]

---

563. *The Effect of Time and Temperature on Potentials Measured with the Glass Electrode.*

By H. Irving and R. J. P. Williams.

Potentials of a glass electrode|buffer|Ag/AgCl system agree with those predicted by the Nernst equation when the temperature is raised progressively, but, on cooling, a hysteresis effect is observed. The implications in the determination of paH are discussed.

When tested on different occasions with fresh portions of the same buffer (0·05M-potassium hydrogen phthalate in 0·5M-potassium chloride), values of $E_{phthalate}$ for the E.M.F., at 20°, of the cell

Ag/AgCl in 0·1M-HCl	Glass membrane	Buffer in 0·1M-KCl	Ag/AgCl in 0·1M-KCl

showed random variations of as much as 4 mv. The same lack of reproducibility characterised similar measurements of E_{borate} with a borate buffer. That changes in the asymmetry potential of the glass electrode were responsible was established by measuring the E.M.F. first with a phthalate buffer and then, immediately after, at the same temperature with the borate buffer. The potential difference

$$\Delta E = E_{phthalate} - E_{borate} = (\boldsymbol{RT}/\boldsymbol{F})\,(\mathrm{paH}_{borate} - \mathrm{paH}_{phthalate})$$

was now found to be constant to within a few tenths of a mv. on each occasion and its magnitude corresponded, within ±0·2 mv., to the value calculated from the known activity exponents of the buffers and the theoretical value at 20° of the gradient $\boldsymbol{RT}/\boldsymbol{F}$ of the plot of ΔE against paH. Similar experiments at other fixed temperatures confirmed that the difference ΔE between consecutive E.M.F. measurements on the above cell when made up at any time with any chosen pair of buffers was accurately reproducible although individual measurements on either buffer separately were subject to a more or less random drift.

A new series of measurements was next carried out as follows. The E.M.F. of the cell was measured as before at one fixed temperature with phthalate and borate buffers in succession. During two minutes the temperature was raised by 5° and, when thermal equilibrium had again been attained, the E.M.F. measurements were repeated on fresh portions of the same phthalate and borate buffers, previously brought to the desired temperature. Over the range 0—40° the

plot of ΔE against T was effectively a straight line of slope 4×10^{-4} v./°c. But if measurements were continued with the two buffers at progressively lower temperatures the values of ΔE at any given temperature were not reproducible and did not correspond with those previously obtained; points for the "cooling" curve sometimes lay on the "heating" curve but more often above it. After some time "normal" values of ΔE were once again obtainable. A similar hysteresis effect could be duplicated by other glass electrodes and other pairs of buffer solutions.

If E_p and E_q are consecutive measurements at any fixed temperature of our cell with buffers of activity exponents paH_p and paH_q it is easy to see that the total variation of ΔE with temperature will be a function compounded of the temperature variation of the hydrogen-ion activity of each buffer, and of the multiplier RT/F. Explicitly, by differentiating the above equation,

$$\partial\Delta E/\partial T = (R/F)(paH_q - paH_p)_T + (RT/F)(\partial paH_q/\partial T) - (RT/F)(\partial paH_p/\partial T)$$
$$= A + B - C$$

Values for the gradients B and C for the borate and the phthalate buffer calculated by Hamer and Acree (*J. Res. Nat. Bur. Stand.*, 1944, **32**, 215) and Manov, DeLollis, Lindvall, and Acree (*ibid.*, 1946, **36**, 543) appear in the third and fourth columns of the Table below, which includes calculated values of A. The agreement between the experimental and calculated values of $\partial\Delta E/\partial T$ is seen to be very satisfactory, the effective constancy of the slope being the result of a somewhat fortuitous compensation of three terms of comparable magnitude.

Similar measurements carried out with a phthalate and a phosphate buffer pair confirmed the previous results, a graph of almost constant slope $3{\cdot}1 \times 10^{-4}$ v./°c. being obtained with rising but not with falling temperatures. The agreement between the calculated and experimental values of $\partial\Delta E/\partial T$ shown in the second section of the Table is scarcely less satisfactory, considering the uncertainty which attaches to the long extrapolations involved in assessing the magnitudes of the terms B and C and the greater sensitivity of the hydrogen-ion activity of phosphate buffers to changes of temperature. In the corresponding measurements with three different hydrochloric acid–potassium chloride buffers no allowance has been made for the (unknown) variation of $paH_{Hg_2Cl_2}$ with temperature, but this must clearly be small. Automatic temperature compensation in most commercial pH-meters compensates only for variations in the term A, and the extent to which errors may be introduced by simultaneous variations due to the terms B and C can be inferred from the Table.

				$\partial\Delta E/\partial T \times 10^4$, v./°c.,						$\partial\Delta E/\partial T \times 10^4$, v./°c.,	
T, °c.	A.	B.	C.	calc.	found.	T, °c.	A.	B.	C.	calc.	found.
Borate.						*Hydrochloric acid* (2).					
20	+104·4	−62·8	+ 2·1	+40	+46	20	−25·3	—	+ 2·1	−27	−33
25	+103·5	−55·6	+ 8·3	+40	+40	25	−25·4	—	+ 8·3	−34	−33
30	+102·3	−51·7	+10·8	+40	+35	30	−25·5	—	+10·8	−36	−40
35	+101·3	−51·4	+12·2	+39	+36	35	−25·7	—	+12·2	−38	−38
40	+100·2	−43·5	+14·9	+42	+40	40	−25·9	—	+14·9	−41	−39
Phosphate.						*Hydrochloric acid* (3).					
16	+56·98	−25·82	+ 1·6	+29·5	+34	20	−6·2	—	+ 2·1	− 8·0	− 8·0
20·5	+56·59	−20·97	+ 2·1	+33·5	+32	25	−6·3	—	+ 8·3	−15	−11
28·5	+56·94	−11·95	+ 9·3	+35·7	+29	30	−6·5	—	+10·8	−17	−15
32·0	+55·67	−10·9	+11·4	+33·4	+31	35	−6·6	—	+12·2	−19	−20
37·5	+55·22	− 6·2	+13·5	+35·5	+31	40	−6·9	—	+14·9	−22	−22
Hydrochloric acid (1).											
20	−44·5	—	+ 2·1	−47	−43						
25	−44·6	—	+ 8·3	−53	−56						
30	−44·8	—	+10·8	−55	−53						
35	−45·0	—	+12·2	−57	−54						
40	−45·2	—	+14·9	−60	−63						

Measurements with a 0·05M-phthalate buffer of paH (25°) 3·932 alternated with those of buffers Q comprising respectively 0·05M-borate of paH (25°) 9·112, M/40-potassium dihydrogen phosphate with M/40-disodium hydrogen phosphate of paH (25°) 6·734, and hydrochloric acid buffers (1), (2), and (3) of paH (25°) 1·681, 2·654, and 3·614. All buffers were 0·1M. with respect to KCl. Columns A, B, and C give the gradients referred to in equation (1) in volts $\times 10^3$ per °c.

There is abundant evidence that the glass electrode can be relied upon for measurements at constant temperature (cf. Dole, "The Glass Electrode," J. Wiley & Sons, New York, 1941). The present work confirms this and shows, moreover, that it is equally reliable even when the

temperature of measurement is varied moderately rapidly, provided always that (*a*) such measurements are made only with an increasing monotonic sequence of temperatures, and (*b*) the intercept of the linear plot of E.M.F. against paH (*i.e.*, the " constant " E_0 of the Nernst equation) is redetermined at each temperature by measurements with one or more buffers of known hydrogen-ion activity. Owing to the relatively large temperature gradient of the quinhydrone electrode (which is, moreover, opposite in sign to that of the Ag/AgCl electrode) glass electrodes containing this internal electrode are unsuitable for measurements of the type recorded above, for the plot of ΔE against T is strongly curved and hysteresis effects were more pronounced. A point of considerable practical importance is the limited degree of efficiency of silvering and chloridising of the internal reference electrodes of some commercial glass electrodes. After but two thermal cycles (20° to 40° and back), one Danish electrode failed completely, and individual electrodes of English manufacture were visibly affected after 50 cycles; others appeared unchanged after as many as 100 cycles.

INORGANIC CHEMISTRY LABORATORY,
SOUTH PARKS ROAD, OXFORD.

[*Received, March* 14*th*, 1950.]

---

564. *Absorption Spectra and Structure of Organic Sulphur Compounds. Part VII. Sulphoxides.*

By H. P. KOCH.

Ultra-violet absorption curves of saturated, $\beta\gamma$-unsaturated, and aromatic sulphoxides in both hydrocarbon and hydroxylic solvents are presented and briefly discussed with reference to electronic interaction of groups. Certain experimental data suggest the possibility of enolisation in the $\beta\gamma$-unsaturated compounds.

IN continuation of previous measurements in this series (Parts I—IV, *J.*, 1949, 387 *et seq.*), the ultra-violet absorption spectra in solution of a representative group of organic sulphoxides have now been determined. Contrary to the behaviour of saturated organic sulphones which are transparent throughout the quartz ultra-violet region, the corresponding sulphoxides display considerable absorption as exemplified by the curve for the *cyclo*hexyl methyl compound shown in Fig. 1. This absorption is markedly enhanced in the $\beta\gamma$-unsaturated sulphoxides such as the methyl β-methylallyl (I) and the diallyl derivatives, which may be compared in Fig. 1 not only with the above saturated sulphoxide but also with a typical olefin, *cyclo*hexene; the comparison shows that electronic interaction occurs between the sulphoxide grouping and the allylic substituent. Further similar shifts of absorption occur in the " conjugated " methyl phenyl and diphenyl sulphoxides. The latter compound has been measured above 2400 A. by Chaix (*Bull. Soc. chim.*, 1933, **53**, 709), in excellent agreement with the present results. There is also remarkable similarity between the spectra of diphenyl sulphoxide and the corresponding selenoxide which is included in Fig. 1. As might be expected, the curves for the phenyl compounds display characteristic shoulders near 2750 A. attributable to the perturbed benzenoid chromophore; the very flat maximum for methyl phenyl sulphoxide near 2350 A. seems to correspond to the weakly selective absorption of saturated sulphoxides near 2100 A., and the more intense bands of the diphenyl derivatives to the well-known strong benzene absorption ($\log \varepsilon \sim 4$) near 2000 A.

The sulphoxide spectrum is subject to considerable solvent effects, consistently with the known tendency of these compounds to form strong hydrogen bonds (cf. Part V, Barnard, Fabian, and Koch, *J.*, 1949, 2442). The greatest absorption occurs in *cyclo*hexane, and successive hypsochromic shifts result from replacing the non-hydroxylic solvent by alcohol and then by water, the additional shift between alcohol and water being relatively less marked. These features are illustrated by the high-intensity region of the methyl 2-methylallyl sulphoxide spectrum shown in Fig. 2. The 2300 A. shoulder of the curve measured in *cyclo*hexane presumably corresponds to the 2100 A. shoulder of *cyclo*hexyl methyl sulphoxide in alcohol (Fig. 1), the displacement being due to the combined effects of allylic substitution and the change in the nature of the solvent. A similar shoulder was observed in an $\alpha\beta$-unsaturated naturally occurring sulphoxide determined in aqueous solution by Schmid and Karrer (*Helv. Chim. Acta*, 1948, **31**, 1017, 1087), whose curve (Fig. 2) is seen to be displaced by some 250—300 A. from that referring to the $\beta\gamma$-unsaturated sulphoxide in the same solvent.

At low intensities ($\log \varepsilon \sim 1$), a second band unexpectedly appears in the spectrum of methyl

2-methylallyl sulphoxide (I) near 2900 A., with solvent effects opposite to those recorded for the main absorption (cf. Fig. 2). As this band was present in several independently prepared and carefully purified samples, it is thought to be characteristic of the allylic compound itself rather than some impurity. A similar band is suggested by the broad tail of the diallyl sulphoxide curve in the same region (Fig. 1). The interesting possibility therefore arises that the long-wave absorption may be due to a trace (of the order of 0·1%) of a conjugated enol form such as (Ia), which might be expected to absorb in this region and be present in low equilibrium concentration. We have not attempted to obtain more positive identification of this chromophore, chiefly because the most obvious approach by way of infra-red detection of a hydroxyl frequency would have doubtful value in such low concentration on account of the extreme tenacity with which bound water is held by the sulphoxide (Barnard, Fabian, and Koch, *loc. cit.*). It may

FIG. 1.

Absorption spectra, in ethanol.

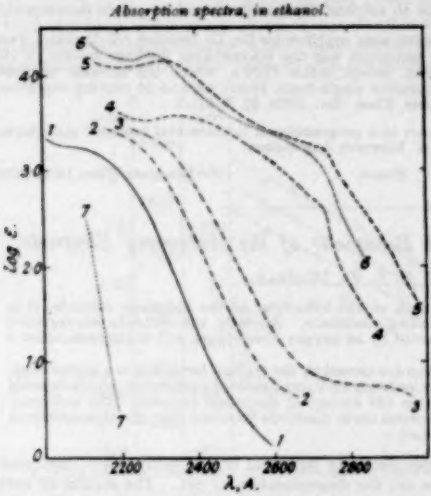


FIG. 2.

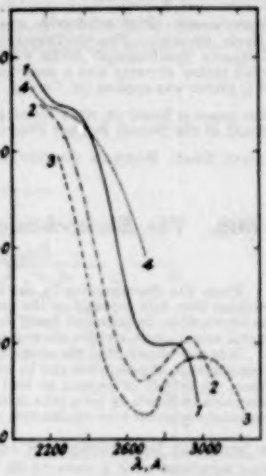


FIG. 1.—1, cyclo*Hexyl methyl sulphoxide.* 2, *Methyl* 2-*methylallyl sulphoxide.* 3, *Diallyl sulphoxide.* 4, *Methyl phenyl sulphoxide.* 5, *Diphenyl sulphoxide.* 6, *Diphenyl selenoxide.* 7, cyclo*Hexene.*

FIG. 2.—*Absorption of methyl* 2-*methylallyl sulphoxide in* (1) cyclo*hexane,* (2) *ethanol, and* (3) *water. Curve* 4 *is absorption of* "*sulphoraphene,*" Me·SO·CH:CH·$[CH_2]_4$·NCS, *in water* (*after Schmid and Karrer,* loc. cit.).

nevertheless be significant that Barnard (*loc. cit.*) observed the occurrence of a violent reaction between phosphoric oxide and $\beta\gamma$-unsaturated, but not saturated, sulphoxides.

CH_2:CMe·CH_2·SOMe (I.) CH_2:CMe·CH:S(OH)·Me (Ia.)

The nature of conjugation in $\alpha\beta$-unsaturated and phenyl sulphones has recently been discussed in Part VI of this series by Koch and Moffitt (*Trans. Faraday Soc.*, in the press). The theoretical conclusions obtained for the sulphones do not necessarily apply to the corresponding sulphoxides, however, without modification; in fact, it would seem likely from the lower degree of symmetry that the conjugating power of the sulphoxide grouping should be rather less. Some interesting experimental evidence on this point is available from the recent work of Eastman and Wagner (*J. Amer. Chem. Soc.*, 1949, **71**, 4089), who found that the 1-oxide (*i.e.*, sulphoxide) derived from certain 3 : 4-dihydroxythiophens was spectroscopically and chemically similar to the parent sulphide, whereas the 1 : 1-dioxide (*i.e.*, sulphone) was distinct and exhibited strong acidity attributable to conjugation of the S–O bonds. The present ultra-violet measurements support the view that some conjugation occurs in $\alpha\beta$-unsaturated and monophenyl sulphoxides, with additional conjugation in the symmetrical diphenyl compound; at the same time, the positive absorption of saturated sulphoxides and the marked chromophore interaction

in βγ-unsaturated derivatives is reminiscent of the behaviour of the corresponding sulphides rather than sulphones. It seems that the sulphoxide grouping has electronic properties intermediate between those of sulphides and sulphones, quite in accordance with the presence of one lone pair of sulphur electrons and one sulphur–oxygen double bond, respectively. Although more fundamental theoretical and experimental investigation of these relationships is evidently required, it is not proposed to develop the subject further in these laboratories.

Added in Proof (*September 11th*, 1950).—Mr. J. P. Teegan and Dr. A. D. Walsh have kindly photographed the vacuum ultra-violet absorption spectrum of a highly purified sample of dimethyl sulphoxide (m. p. 16°) prepared by Dr. D. Barnard. A first absorption region at *ca.* 1900 A. was followed by a more intense region, 1750—1550 A., in which some discrete bands could be observed. A third intense region below 1350 A. apparently contained a series of Rydberg bands superimposed on a background of continuous absorption, but the discrete bands in this region may have been due to sulphur dioxide produced by photo-decomposition.

Experimental.—Pure sulphoxide specimens were supplied by Dr. D. Barnard (cf. Barnard, Fabian, and Koch, *loc. cit.*). The spectrographic technique was the conventional Spekker method, a Hilger small quartz spectrograph being employed, except below 2100 A. where the Spekker photometer absorbed rather strongly and a semi-quantitative single-beam Henri method of varying exposures on Ilford Q plates was applied (cf. Carr, *J. Amer. Chem. Soc.*, 1929, **51**, 3051).

This paper is based on work forming part of a programme of fundamental research undertaken by the Board of the British Rubber Producers' Research Association.

Tewin Road, Welwyn Garden City, Herts. [*Received, June 14th*, 1950.]

---

565. *The Electrochemical Behaviour of the Antimony Electrode.*

By S. E. S. El Wakkad.

From the discrepancies in the reports on the behaviour of the antimony electode, it is evident that this depends on the prevailing conditions. Recently, the electrode was regarded as irreversible, its potential being governed by an oxygen overvoltage, and it has been called a metal–metal oxide–oxygen electrode.

It is now shown that the irregularities are caused by the gradual formation of a higher oxide (tetroxide) on the electrode and by its exceedingly slow attainment of equilibrium, which depends upon the supply of oxygen as well as on the surface of the metal exposed. The antimony electrode is shown to be a true metal–metal oxide electrode provided that the measurements recorded represent true equilibrium values.

Much work has been carried out on the electrode potential of antimony when immersed in aqueous solutions with a view to its use for the determination of pH. The results of various workers differ widely, and individual values are greatly dependent on the nature of the conditions. Many suggestions as to the cause of this behaviour have been advanced, and although in many cases the presence of dissolved oxygen has been recognised as a fundamental factor influencing the electrode potential, it seems that no attempt has been made to define satisfactorily the real nature of the effect of this gas on the antimony electrode potential.

The behaviour of the antimony electrode (stick and plated) as an indicator electrode for hydrogen ion activity was recently re-examined by Tourky and Mousa (*J.*, 1948, 752); since they found that the E_0 values of their electrodes, as well as those of most previous authors, fluctuated between 0·165 and 0·290 v. as compared with the value of 0·150 v. obtained with the powdered antimony electrode for the system $Sb–Sb_2O_3$, they concluded that the electrode behaves irreversibly only when in the massive form, its behaviour being governed by an oxygen overvoltage effect due to the persistence on its surface of oxygen doublets. The electrode was therefore called a metal–metal oxide–oxygen electrode.

Some experiments are now reported showing that the antimony electrode, whether in the powdered, massive, or plated form, is reversible; further, that both the fluctuations and the drift observed in the E_0 values by various authors can largely be explained by the gradual formation of a higher oxide (tetroxide) on the electrode and by its exceedingly slow rate of attainment of equilibrium, which depends upon the supply of oxygen and on the surface of metal exposed. When this equilibrium is reached, it corresponds to the reversible value of the system $Sb_2O_3–Sb_2O_4$. The limits of the applicability of the antimony electrode as an indicator electrode for hydrogen-ion activity are defined, and the importance of obtaining a calibration curve for the electrode before use is emphasised.

Experimental.

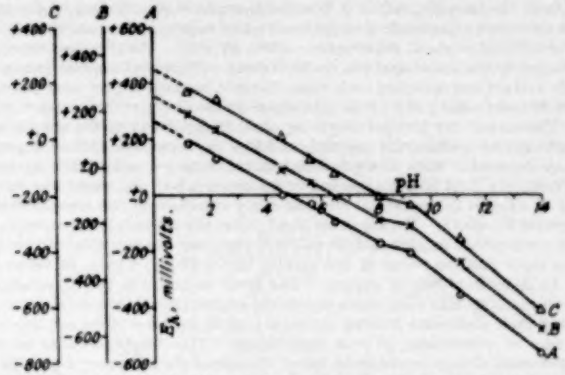
Electrodes.—The antimony electrodes used were of 3 types: (a) *Stick electrode.* This was a rod of pure antimony (B.D.H.) 1·5 cm. long and 0·5 cm. in diameter. (b) *Plated electrode.* This was prepared according to the directions of Shoch and Brown (*J. Amer. Chem. Soc.*, 1916, **38**, 1660); the antimony was deposited on a platinum wire of apparent area 0·05 cm.². (c) *Powdered electrode.* This was the B.D.H. sample which had been shaken with the solution for some time and then used directly.

The solutions in which the antimony electrodes were examined were buffers covering the pH range 1·2—13·9, *viz.*, potassium chloride–hydrochloric acid, acetic acid–sodium acetate, disodium hydrogen citrate–sodium hydroxide, boric acid–borax, and sodium carbonate–hydrochloric acid buffer mixtures (Britton, "Hydrogen Ions," London 1929, pp. 181 *et seq.*). For the extreme alkaline pH value N-sodium hydroxide was used.

The electrical measurements were carried at 20° ± 0·05°, a saturated calomel electrode being used as the reference half-cell.

Results and Discussion.

With the three types of electrodes it was possible to differentiate between two potentials, *viz.*, pseudo-equilibrium values which were usually obtained within 3—6 hours, and the steadier values obtained within 72 hours with the massive electrodes and within 120—144 hours



A, Stick antimony electrode. B, Plated antimony electrode. C, Powdered antimony electrode.

with the powder electrode. The pseudo-equilibrium values were approximately the same for the stick and the plated electrode and both were on the average about 0·03—0·05 v. higher than for the powder electrode. In all the cases, the pseudo-equilibrium values slowly became more positive with time. The rate of this drift gradually decreased, becoming fairly constant after the periods noted above. The figure shows the steadier potential–pH curves for the three types of electrode, and it is seen that the potential of the antimony electrode is a linear function of the pH from ~1 to ~8 and then from pH 9 to 13·9. A break always occurred between pH 8 and 9. The E_0 values (values at pH 0) were 0·255, 0·260, and 0·250 v. for the rod, plated, and powder forms, respectively.

The electromotive behaviour of antimony oxides in 0·1N-hydrochloric acid, studied by Hickling and El Wakkad, will be published elsewhere. The results obtained give the following E_0 values for the corresponding systems: Sb–Sb_2O_3 +0·15 v., Sb_2O_3–Sb_2O_4 +0·54 v., Sb_2O_4–Sb_2O_5 +0·59 v., Sb_2O_3–Sb_2O_5 +0·67 v., and it is obvious that the E_0 values obtained with the antimony electrodes are different from any of these.

A survey of the literature on the antimony electrode (see Tourky and Mousa, *loc. cit.*) reveals that only in two out of 23 studies is the E_0 value as low as 0·150 v. Careful examination of these two cases shows that the metal used was in the form of powder and the electrodes as well as the solutions were not freely exposed to atmospheric oxygen. On the other hand, the higher E_0 values were mostly obtained with massive electrodes and in solutions freely exposed to atmospheric oxygen, and in this case a continuous drift with time in a more positive direction was noticed and the E_0 values fluctuated between two widely separated extremes.

The fluctuations in E_0 values and the drift with time suggest that in these cases the measured

potentials do not represent final equilibrium. The fact that the drift is in a more positive direction indicates that a higher oxide is being formed and that the disturbance is probably due to the very slow approach of the electrode to its final equilibrium value. This view was further substantiated by measuring the potential of the plated antimony electrode in 0·1N-hydrochloric acid and waiting until the steadier potential was reached; then by bubbling oxygen continuously through the solution, it was found that the drift in potential continued though very slowly towards the more positive direction. For instance, after 3 days the change in potential was ~30 mv., after a week ~40 mv., and after 14 days ~220 mv., so reaching the constant value of 0·490 v. This final potential value agrees satisfactorily with the value of the system Sb_2O_3–Sb_2O_4 at the corresponding pH. It was also noticed, when measuring the potential of the system Sb–Sb_2O_3 in 0·1N-hydrochloric acid and then adding small amounts of either Sb_2O_4 or Sb_2O_5, that the potential varied only by ~90 mv. within the first 24 hours and by ~120 mv. after 42 hours, although the realisation of the systems Sb–Sb_2O_3–Sb_2O_4 or Sb–Sb_2O_3–Sb_2O_5 would necessitate an increase of ~400 or 570 mv., respectively. On the other hand, when powdered antimony was added to Pt–Sb_2O_3–Sb_2O_4 or Pt–Sb_2O_3–Sb_2O_5 the potential at once decreased to ~0·100 v., tending towards that of the Sb–Sb_2O_3 system.

From these observations one can conclude that when the antimony electrode is dipped in aqueous solutions, the trioxide, which is the stable oxide at the surface of the metal, is first formed. This oxide in the presence of oxygen and water can be further oxidised to the tetroxide or the pentoxide (Wulff *et al.*, *Z. Elektrochem.*, 1935, **41**, 542). At the same time the Sb^{IV} and Sb^{V} can be reduced by the metal again to the Sb^{III} state. Thus we have two processes operating at the electrode surface and opposing each other, the first tending to give more positive potential values and the second tending to push it back again to the comparatively negative potential of the trioxide. The rate of the first process is expected to depend upon the amount of oxygen to which the electrode and solution are exposed, and that of the second process depends upon the metallic surface exposed. With the powdered metal, where a comparatively large metallic surface is exposed, the drift is not expected to be appreciable, and when the electrode is not freely exposed to oxygen the potential remains fairly constant at the comparatively negative value of the system Sb–Sb_2O_3. On the other hand, when the metal is in the massive form and in the presence of atmospheric oxygen, a drift will take place and the potential will tend to, but may not, attain the more positive value of the system Sb_2O_3–Sb_2O_4, which, as before, can only be reached after 14 days' bubbling of oxygen. The great variation in the E_0 values obtained by different authors confirms this view, since one would expect that their solutions were differently aerated and that their electrodes differed in shape, and in our view these are important factors affecting the rate of attainment of true equilibrium. This treatment also explains why a calibration curve must always be obtained before the use of the antimony electrode as indicator for hydrogen-ion activity in aerated solutions.

From all these facts it is quite clear that the assumption of the presence of oxygen doublets on the massive antimony electrode is unnecessary and that the antimony electrode is a true metal–metal oxide electrode provided that our measurements represent true equilibrium values. Further, Tourky and Mousa's assumption of the presence of oxygen doublets necessitates that the Sb_2O_3 film formed over the surface of the antimony is unimolecular and very protective, whereas Hickling and El Wakkad's study of the anodic behaviour of antimony showed that the unimolecular film of Sb_2O_3 formed on the surface of the metal is not at all protective and the film reaches a thickness of several molecules.

The break always noticed at about pH 8—9 may be attributed, as in other cases of potential–pH curves of metal–metal oxide electrodes (Tourky and El Wakkad *J.*, 1948, 740; El Wakkad and Salem, *J. Phys. Colloid Chem.*, 1950, in the press), to the position of the isoelectric point of Sb_2O_3, which lies at about pH 8·6 (Tourky and Mousa, *J.*, 1948, 755). Tourky and Mousa (*loc. cit.*, p. 758) attributed the breaks in their potential–pH curves to different types of dissociation of $Sb(OH)_3$. Such an assumption, however, is not justifiable since, whatever the kind of the dissociation of $Sb(OH)_3$, so long as the different ionic species are in equilibrium with each other the potential must be the same. Only at the isoelectric point, where the oxide or hydroxide can be considered as dissociating neither as acid nor as base, can one expect anomalous behaviour: before or after this, the normal trend of the potential–pH curves of the metal–metal oxide must exist.

The author thanks Dr. A. Hickling for the facilities he provided during the course of this work.

UNIVERSITY OF LIVERPOOL. [*Received, June 16th*, 1950.]

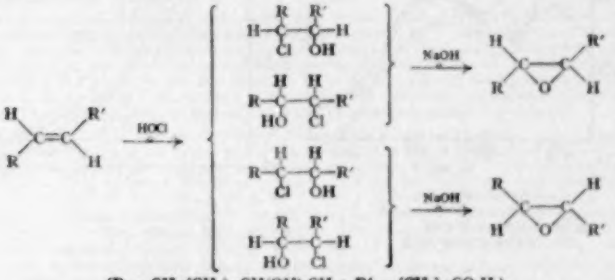
566. trans-8 : 9-*Epoxy*-11-*ketoheptadecane*-1-*carboxylic Acid and* cis-10 : 11-*Diketoheptadec*-8-*ene*-1-*carboxylic Acid, with Some Observations on the Ultra-violet Absorption Spectra of These and Related Compounds.*

By George King.

trans-8 : 9-Epoxy-11-ketoheptadecane-1-carboxylic acid (λ-ketoelaidic acid oxide), m. p. 84°, has been prepared by chromic acid oxidation of a mixture of diastereoisomeric ricinelaidic acid oxides, and its properties have been studied. The compound, m. p. 112·5°, resulting from the autoxidation of λ-keto-oleic acid and previously thought to be the corresponding epoxide, has now been identified as *cis*-10 : 11-diketoheptadec-8-ene-1-carboxylic acid (αλ-diketo-oleic acid). The absorption spectra of these and certain related compounds have been examined.

It has already been shown (King, *Nature*, 1949, **164**, 706; Swern *et al.*, *Analyt. Chem.*, 1947, **19**, 414) that the absorption of hydrogen chloride from ether or dioxan by simple 1 : 2-epoxides is more or less quantitative. Nothing is known, however, of the effect on this absorption of the presence of a neighbouring carbonyl group or double bond. In the search for suitable keto-epoxides, it was decided to attempt the preparation of the λ-keto-derivatives of oleic acid oxide and elaidic acid oxide, since these might be synthesised from the readily accessible ricinoleic acid and ricinelaidic acid respectively. A study of the properties of these and related substances was particularly desirable in view of their possible occurrence in autoxidation processes (Ellis, *J.*, 1950, 9).

Ricinelaidic acid oxide, m. p. 64°, was prepared by Smit (*Rec. Trav. chim.*, 1930, **49**, 681) by oxidising methyl ricinelaidate with perbenzoic acid and hydrolysing the product. A similar substance, m. p. 64—67°, has now been obtained from ricinelaidic acid by the addition of hypochlorous acid, followed by treatment of the chlorohydrins with dilute alkali. The product is undoubtedly a mixture of diastereoisomeric epoxides (cf. King, *J.*, 1949, 1817), and is optically active.



(R = CH_3·$[CH_2]_5$·CH(OH)·CH_2; R′ = $[CH_2]_7$·CO_2H.)

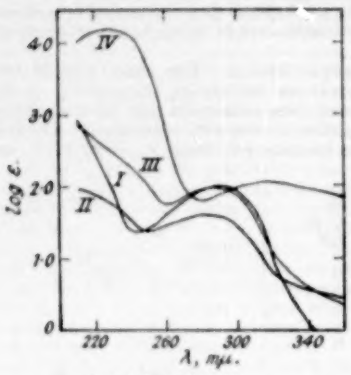
Mild oxidation of the epoxide mixture with chromium trioxide in acetic acid affords (±)-*trans*-8 : 9-epoxy-11-ketoheptadecane-1-carboxylic acid (λ-ketoelaidic acid oxide), m. p. 84° (oxime, m. p. 78°), which was found to absorb only 70% of the theoretical amount of hydrogen chloride from dioxan or ether. So low a result must be attributed to the presence of the carbonyl group, since ricinelaidic acid oxide itself absorbs hydrogen chloride nearly quantitively under similar conditions to form a mixture of chlorohydrins, m. p. 86—91°. This observation clearly imposes a serious limitation on the accuracy of epoxide determinations based on this principle.

λ-Ketoelaidic acid oxide does not absorb ultra-violet light strongly at wave-lengths exceeding 200 mμ., but exhibits a weak band in ethanol at 282 mμ. ($\varepsilon_{max.}$ 38). Slow distillation of the epoxide with N- or 0·1N-sodium hydroxide affords a 12% yield of octan-2-one, to be compared with 26—34% of the same ketone given by λ-keto-oleic (or -elaidic) acid under similar conditions (Ellis, *loc. cit.*). In the pyrazoline test (*idem*, *ibid.*), hitherto regarded as specific for the groups ·CO·CH:CH· and ·CO·CH_2·CH:CH·, it gives an intense violet colour even in the cold. In common with other ketones containing the ·CO·CH_3· group, it develops a purple colour with 3 : 5-dinitrobenzoic acid in aqueous-ethanolic sodium hydroxide, although the test is more sensitive for

λ-ketoelaidic acid and still more so for λ-keto-oleic acid, of which 1 μg. in 0·1 ml. of ethanol may just be detected. λ-Ketoelaidic acid oxide reduces Fehling's solution slowly on boiling, probably on account of the formation of reducing substances on alkaline hydrolysis, a view which is supported by the fact that the readily hydrolysable λ-keto-oleic and -elaidic acids reduce Fehling's solution rapidly, whereas ricinelaidic acid and its epoxide are without action.

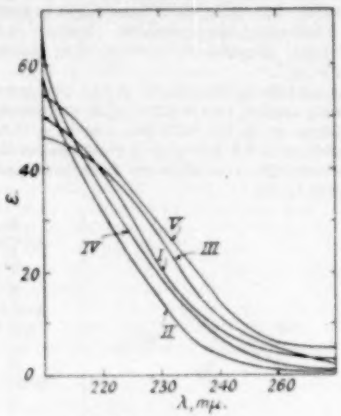
Efforts to prepare the isomeric *cis*-8 : 9-epoxy-11-ketoheptadecane-1-carboxylic acid (λ-keto-oleic acid oxide) from λ-keto-oleic acid by way of the chlorohydrins or by oxidation with perbenzoic acid have proved unsuccessful. The alternative route from ricinoleic acid by way of its epoxide appears equally unsatisfactory. It was observed by Ellis (*loc. cit.*) that λ-keto-oleic acid readily undergoes autoxidation in air at warm room temperature to yield a peroxide of unknown constitution, together with a considerable proportion of crystalline product, m. p. 112·5°, which was thought to be an epoxyketostearic acid, but whose constitution remained uncertain in view of the fact that it could not be hydrolysed to the corresponding dihydroxyketostearic acid (private communication). Evidence has now been adduced to show that this crystalline product is the unsaturated diketo-acid, *cis*-10 : 11-diketoheptadec-8-ene-1-carboxylic acid (κλ-diketo-oleic acid), the methylene group in position 10 having undergone autoxidation.

Fig. 1.



I. λ-Ketoelaidic acid.
II. λ-Ketoelaidic acid oxide.
III. λ-Keto-oleic acid.
IV. κλ-Diketo-oleic acid.

Fig. 2.



I. Oleic acid oxide.
II. Elaidic acid.
III. Elaidic acid oxide.
IV. Ricinelaidic acid.
V. Ricinelaidic acid oxide.

κλ-Diketo-oleic acid has a nearly theoretical iodine value and gives a disemicarbazone and a 2 : 4-dinitrophenylosazone. It absorbs a small amount of hydrogen chloride from organic solvents, a property which, as will be shown elsewhere, is shared by certain other compounds containing the group ·CH:CH·CO· or ·CH:CH·CH_2·CO·. The presence of the chromophore ·CO·CO·CH:CH· is strongly supported by spectroscopic evidence, since the ultra-violet absorption spectrum in ethanol, unlike that of λ-ketoelaidic acid oxide, exhibits an intense absorption band at λ 228 mμ. ($\varepsilon_{max.}$ 16,000) as well as a weak subsidiary band at λ 318 mμ. ($\varepsilon_{max.}$ 115). The spectrum thus closely resembles those of crotonaldehyde and diacetylethylene, CH_3·CO·CH:CH·CO·CH_3 (Bowden *et al.*, *J.*, 1946, 39; Braude, *J.*, 1945, 490), containing conjugated systems involving one or more carbonyl groups.

For the purposes of comparison, the ultra-violet light absorption, in ethanol, of a number of other related compounds has also been investigated. The results (Figs. 1 and 2) are summarised in the following Table. Of the compounds examined, only the keto-acids exhibit well-defined maxima and minima within the wave-band 210—400 mμ. The remainder absorb ultra-violet light to an insignificant extent at wave-lengths exceeding 230 mμ., and, as might be expected, epoxidation of the ethylenic acids appears to reduce the intensity of absorption. The absorption

	$\varepsilon_{240\ m\mu}$.*	$\lambda_{max.}$ ($m\mu$.).	$\varepsilon_{max.}$	$\lambda_{min.}$ ($m\mu$.).	$\varepsilon_{min.}$
λ-Ketoelaidic acid, m. p. 72°	925	287	100	244	27
λ-Ketoelaidic acid oxide, m. p. 84°	97	282	38	250	25
λ-Keto-oleic acid, m. p. 40°	800	285	93	260	37
αλ-Diketo-oleic acid, m. p. 112·5°	10,750	228	16,000	280	62
		318	115		
Elaidic acid, m. p. 44·5°	58	—	—	—	—
Elaidic acid oxide, m. p. 55·5°	46	—	—	—	—
Oleic acid oxide, m. p. 59·5°	50	—	—	—	—
Ricinelaidic acid, m. p. 52°	70	—	—	—	—
Ricinelaidic acid oxide, m. p. 64—67° ...	54	—	—	—	—

* Lowest wave-length recorded.

spectra of oleic and elaidic acid epoxides have already been investigated by Holman *et al.* (*J. Amer. Chem. Soc.*, 1945, **67**, 1285), but only down to a wave-length of 240 mμ. It is noteworthy that the values here found for the molecular extinction coefficient of elaidic acid, which was very carefully purified, are somewhat lower than those recorded by Rusoff *et al.* (*ibid.*, p. 673).

Experimental.

Ricinelaidic Acid Oxides (8 : 9-*Epoxy*-11-*hydroxyheptadecane*-1-*carboxylic Acids*).—Dilute hydrochloric acid was added dropwise, with vigorous shaking, to a solution of ricinelaidic acid (30 g.) in 1·3*u*-sodium hypochlorite (115 ml.) and water (1·5 l.) until the solution was slightly acid. Free chlorine and excess of hypochlorous acid were destroyed by addition of aqueous sodium sulphite, the solution was further acidified with hydrochloric acid, and the sticky mixture of chlorohydrins washed by decantation. The product was dissolved in N-sodium hydroxide (300 ml.), and the solution left for several hours and then boiled for a few minutes. Acidification of the cooled solution with dilute sulphuric acid, extraction with ether, and precipitation with 2 vols. of N-hexane afforded a mixture of stereoisomeric ricinelaidic acid oxides (11·5 g.; m. p. 58—61°), which on further crystallisation from ether–hexane and from ethanol separated as thin, rod-like plates (7·5 g.), m. p. 64—67°, $[\alpha]_D^{20}$ in ethanol $-22°$ ($l = 2$, $c = 1·0$) (Found : equiv., 314; C, 68·5; H, 10·6; oxiran-O, 4·9%. Calc. for $C_{18}H_{34}O_4$: equiv., 314 : C, 68·8; H, 10·9; oxirane-O, 5·1%). Hydrolysis of the epoxides with boiling N-sodium hydroxide for 5 hours gave a 30% yield of 8 : 9 : 11-trihydroxyheptadecane-1-carboxylic acid (probably a mixture of two stereoisomers), m. p. 136—137·5°.

Chlorodihydroxystearic Acids from Ricinelaidic Acid Oxides.—Concentrated hydrochloric acid (10 ml.) was shaken with ricinelaidic acid oxides (6·5 g.) in ether (120 ml.) for 1 hour, after which the washed and dried ethereal solution was treated with 2 vols. of N-hexane and cooled at 0°. The mixture of 8-chloro-9 : 11-dihydroxy- and 9-chloro-8 : 11-dihydroxy-heptadecane-1-carboxylic acids separated from ether–hexane as needles (2·2 g.), m. p. 86—91° (Found : C, 61·6; H, 10·0; Cl, 9·8%; equiv., 352. Calc. for $C_{18}H_{35}O_4Cl$: C, 61·6; H, 10·1; Cl, 10·1%; equiv., 351), from which the original epoxides were recovered in good yield on treatment with 2N-sodium hydroxide at room temperature for 2 hours.

λ-*Ketoelaidic Acid Oxide* (trans-8 : 9-*Epoxy*-11-*ketoheptadecane*-1-*carboxylic Acid*.—A solution of chromium trioxide (3 g.) in water (6 ml.) and acetic acid (16 ml.) was added gradually to ricinelaidic acid oxides (10 g.) in acetic acid (80 ml.), the temperature being kept below 15°. The solution was then left at room temperature for 1½ hours, diluted and cooled. λ-*Ketoelaidic acid oxide* crystallised from ethanol in rhombic and hexagonal plates (4 g.), m. p. 84° (Found : C, 69·2; H, 10·4; oxiran-O, 3·7%; equiv., 311. $C_{18}H_{32}O_4$ requires C, 69·2; H, 10·3; oxiran-O, 5·1%; equiv., 312), sparingly soluble in ether at 0° and rather sparingly soluble in warm light petroleum. The *oxime* crystallised from ethanol in long, thin rhombic plates, m. p. 78° (Found : N, 4·4%; equiv., 327. $C_{18}H_{33}O_4N$ requires N, 4·3%; equiv., 327).

λ-Ketoelaidic acid oxide slowly reduced boiling Fehling's solution and developed a purple colour with 3 : 5-dinitrobenzoic acid in aqueous-ethanolic sodium hydroxide. It also gave the pyrazoline test (Ellis, *loc. cit.*) in the cold : thus 0·1 mg., rubbed with a *trace* of phenylhydrazine on a glass slide and then treated with 1 drop of a 5% (w/v) solution of sodium nitrite in sulphuric acid, gave immediately an intense violet colour which persisted for at least 5 minutes. Under these conditions, λ-keto-oleic acid gave no definite purple or violet colour. When slowly distilled with N- or 0·1N-sodium hydroxide, λ-ketoelaidic acid oxide gave a yield of *ca.* 12% of octan-2-one (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 61°); the remaining hydrolysis products reduced Fehling's solution, gave a mixture of solid products when treated with 2 : 4-dinitrophenylhydrazine, and contained no epoxide, but were not further identified. The epoxide reacted readily with 2 : 4-dinitrophenylhydrazine to give an oil.

λ-*Keto-oleic* (cis-11-*Ketoheptadec*-8-*ene*-1-*carboxylic*) *Acid*.—This acid, prepared from ricinoleic acid substantially as described by Ellis (*loc. cit.*), crystallised from N-hexane in long, thin plates, m. p. 40° [Found : C, 72·3; H, 10·8%; equiv., 295; I.V., (Wijs, 1 hour), 131. Calc. for $C_{18}H_{32}O_2$: C, 72·9; H, 10·9%; equiv., 296; I.V., 85·6]. 1 Ml. of a mixture of 2 vols. of 1% ethanolic 3 : 5-dinitrobenzoic acid and 1 vol. of 10% aqueous sodium hydroxide, added to 0·1 ml. of ethanol containing 0·1 mg. of λ-keto-oleic acid, developed a deep purple colour within a few minutes. As little as 1 μg. of the keto-acid could be detected by this means, the test being about 100 times more sensitive for the keto-acid than for octan-2-one.

α*λ*-*Diketo-oleic* (cis-10 : 11-*Diketoheptadec*-8-*ene*-1-*carboxylic*) *Acid*.—λ-Keto-oleic acid (6 g.), melted and absorbed on filter paper (12 × 50 cm.), was incubated in air at 37° for 5 days. The autoxidised product was extracted with light petroleum (75 ml.; b. p. 40—60°) at room temperature and then with several lots of boiling ethanol (100 ml. in all). The latter, diluted with ½ vol. of water and cooled at 0°, deposited α*λ*-*diketo-oleic acid* (1·5 g.), which crystallised from ethanol in nearly colourless hexagonal

plates, m. p. 112·5° (Found: C, 69·5; H, 9·6%; equiv., 308; I.V., 78·3. $C_{18}H_{36}O_4$ requires C, 69·6; H, 9·7%; equiv., 310; I.V., 81·7). The *disemicarbazone* separated as a canary-yellow microcrystalline powder, m. p. 212° (decomp.), very sparingly soluble in all the usual solvents (Found: C, 56·5; H, 8·4; N, 20·8. $C_{20}H_{42}O_4N_6$ requires C, 56·6; H, 8·5; N, 19·8%). The 2 : 4-*dinitrophenylosazone* crystallised from ethanol–chloroform in small bright red rods, m. p. 154° (softening at 140°) (Found: N, 16·6. $C_{30}H_{42}O_{10}N_8$ requires N, 16·7%), and gave an intense violet colour with ethanolic sodium hydroxide.

Diketo-oleic acid reduced Fehling's solution readily on heating and gave a deep red colour in the dinitrobenzoic acid test. Its solution in aqueous sodium hydroxide had a yellow colour, intensified on boiling, with decomposition of the diketo-acid but without the formation of volatile ketone. In the pyrasoline test in the cold it gave a transient red colour, changing to blue, green, and yellow-brown. Both λ-keto- and αλ-diketo-oleic acid absorbed a little hydrogen chloride from organic solvents, giving apparent oxirane-oxygen values of 0·5—0·75%. The diketo-acid in ethanol gave an absorption band of high intensity in the ultra-violet at 228 mμ. and a subsidiary band at 318 mμ.

Elaidic acid, crystallised repeatedly from acetic acid and from methanol, had m. p. 44·5° (Found: I.V., 90·0; equiv., 282·5. Calc. for $C_{18}H_{34}O_2$: I.V., 89·9; equiv., 282·5). Ricinelaidic acid was prepared by thoroughly stirring a mixture of freshly prepared ricinoleic acid (60 ml.) with concentrated nitric acid (4 ml.) and powdered sodium nitrite (2 g.) and leaving it for 48 hours. The semi-crystalline mass was drained on a Buchner funnel, washed with a little cold light petroleum, and crystallised successively from methanol, n-hexane, and again from methanol, giving the pure acid (36 g.), m. p. 52° (Found: equiv., 298·7. Calc. for $C_{18}H_{34}O_3$: equiv., 298·5). Oleic acid oxide, m. p. 59·5°, was obtained from dihydroxy-stearic acid, m. p. 132° (King, *J.*, 1942, 390), and elaidic acid oxide, m. p. 55·5°, from elaidic acid by the hypochlorous acid method (King, *J.*, 1949, 1820). λ-Ketoelaidic acid, m. p. 73°, was prepared from ricinelaidic acid (Ellis, *loc. cit.*) (Found: equiv., 295·1. Calc. for $C_{18}H_{32}O_3$: equiv., 295·1).

Ultra-violet Absorption Spectra.—These were measured in ethanol, a Model S.P.500 Unicam Spectrophotometer being used.

St. Mary's Hospital Medical School, London, W.2. [*Received, June 21st*, 1950.]

NOTES.

The Preparation of Some 1-*Chloroalkane*-1-*carboxylic Acids.*

By R. H. Horn, R. B. Miller, and S. N. Slater.

In the course of a preliminary study of certain aspects of the Darzens glycide ester synthesis, using the esters of chlorinated long-chain fatty acids, it was found that the purity of the chloro-ester is of critical importance. It became necessary therefore to develop a satisfactory method of preparing quantities of authentic 1-chloroalkane-1-carboxylic acids. The work of Guest *et al.* (*J. Amer. Chem. Soc.*, 1944, **66**, 2074; 1947, **69**, 300) has shown that the only satisfactory general method is that involving chlorination of an alkylmalonic acid followed by decarboxylation (Cloves, *Annalen*, 1901, **319**, 357; Staudinger, Anthes, and Schneider, *Ber.*, 1913, **46**, 3539; Blaise, *Bull. Soc. chim.*, 1914, **15**, 666), and our experience confirms this conclusion. By use of this method we have prepared a series of 1-chloroalkane-1-carboxylic and -1 : 1-dicarboxylic acids and their esters, amides, and anilides, the results being summarised in the tables.

1-*Chloroalkane*-1 : 1-*dicarboxylic acids.*

Alkane.	Formula.	Cl, %. Found.	Cl, %. Calc.	Equiv. Found.	Equiv. Calc.	M.p.*
Propane	$C_5H_7O_4Cl$	20·9	21·3	81·4	83·2	101—103° (*a*)
Pentane	$C_7H_{11}O_4Cl$	17·9	18·3	97·4	97·2	94—96
Heptane	$C_9H_{15}O_4Cl$	15·7	16·0	111·3	111·2	118—119·5
Nonane	$C_{11}H_{19}O_4Cl$	14·0	14·3	124·2	125·2	95—97
Undecane	$C_{13}H_{23}O_4Cl$	12·7	12·7	140·0	139·2	95—96·5

* M. p.s were taken in a bath preheated to about 5° below the recorded figures.

(*a*) Cloves (*loc. cit.*) gives 102—103°; Blaise (*loc. cit.*) 106—107°; Staudinger *et al.* (*loc. cit.*) 101—102°.

1-*Chloroalkane*-1-*carboxylic acids.*

Alkane.	Formula.	Cl, %. Found.	Cl, %. Calc.	Equiv. Found.	Equiv. Calc.	B. p./mm.	n_D^{20}.	d_4^{20}.
Propane	$C_4H_7O_2Cl$	28·9	29·2	125·0	122·5	98°/13·5 (*a*)	1·435	1·189
Pentane	$C_6H_{11}O_2Cl$	23·5	23·6	150·8	150·5	122°/12 (*b*)	1·441	1·100
Heptane	$C_8H_{15}O_2Cl$	19·9	19·9	180·0	178·5	155°/10 (*c*)	1·446	1·049

		C, %. Found.	C, %. Reqd.	H, %. Found.	H, %. Reqd.	Cl, %. Found.	Cl, %. Reqd.	Equiv. Found.	Equiv. Reqd.	M. p.	B. p./mm.
Nonane	$C_{10}H_{19}O_2Cl$	58·4	58·1	9·28	9·20	17·2	17·3	203·0	206·5	23—25°	165°/10 *
Undecane	$C_{12}H_{23}O_2Cl$	61·8	61·4	10·2	9·81	15·0	15·2	234·3	234·5	35—38°	183—184/10

(*a*) Blaise (*loc. cit.*) gives 109·5°/24 mm.; Cloves (*loc. cit.*) 101°/15 mm.

(*b*) Levene and Haller (*J. Biol Chem.*, 1929, **83**, 591) gives 80—95°/1 mm.; Guest (*loc. cit.*) 102—107°/4 mm.

(*c*) Guest (*loc. cit.*) gives 140—145°/4 mm. * n_D^{20} 1·450; d_4^{20} 1·013.

Ethyl esters of 1-*chloroalkane*-1-*carboxylic acids.*

Alkane.	Formula.	C, %. Found.	C, %. Reqd.	H, %. Found.	H, %. Reqd.	B.p./mm.	n_D^{20}.	d_4^{20}.
Propane	$C_6H_{11}O_2Cl$	48·0	47·8 •	7·56	7·31 •	56—57°/12 (*a*, *b*)	1·418 (*a*)	1·050 (*a*, *b*)
Pentane	$C_7H_{13}O_2Cl$	53·7	53·8	8·17	8·40	77—78/10	1·426	1·007
Heptane	$C_{10}H_{19}O_2Cl$	58·5	58·1	9·56	9·20	132·5—135/10	1·432	0·982
Nonane	$C_{12}H_{23}O_2Cl$	61·5	61·4	9·88	9·81	136·5—137·5/10	1·436	0·939
Undecane	$C_{14}H_{27}O_2Cl$	64·4	64·0	10·3	10·3	161—165/15 (*c*)	1·439	0·914

(*a*) Henry (*Chem. Zentr.*, 1898, II, 273) gives b. p. 163—164°, n 1·4243, d^{15} 1·055.
(*b*) Markownikoff (*loc. cit.*) gives b. p. 156—160°, $d^{17·5}$ 1·063.
(*c*) Darzens (*loc. cit.*) gives 132—133°/4 mm. • Calculated (not " required ") values.

Derivatives of 1-*chloroalkane*-1-*carboxylic acids.*

Alkane.	Amides. Formula.	N, %. Found.	N, %. Reqd.	M. p.	Anilides. Formula.	N, %. Found.	N, %. Reqd.	M. p.
Propane	C_4H_8ONCl	12·0	11·5	75·5—76°	$C_{10}H_{12}ONCl$	7·3	7·1	74—76°
Pentane	$C_5H_{10}ONCl$	9·6	9·4	57·5—58·2				
Heptane	$C_8H_{16}ONCl$	8·0	7·9	70—71				
Nonane	$C_{10}H_{20}ONCl$	6·4	6·8	74—74·5	$C_{16}H_{24}ONCl$	5·1	5·0	38—40
Undecane.....	$C_{12}H_{24}ONCl$	6·2	6·0	79—79·5	$C_{18}H_{28}ONCl$	4·1	4·5	50—52

Experimental.—1-*Chloroalkane*-1 : 1-*dicarboxylic acids.* The appropriate alkane-1 : 1-dicarboxylic acids were readily chlorinated, by the method of Staudinger, Anthes, and Schneider (*loc. cit.*). A typical experiment was as follows: nonane-1 : 1-dicarboxylic acid (80 g.) was dissolved in absolute ether (240 c.c.), and sulphuryl chloride (51 g.) was dropped in. The mixture was heated under reflux for 3 hours, washed with water (5 c.c.), dried, and evaporated. The acid was crystallised from toluene–light petroleum (b. p. 40—70°); yield, 67 g. (71%). If impure benzene or toluene is used in these crystallisations (especially with the lower members of the series), dissolution of the acid is accompanied by strong discoloration: 1-chloropropane-1 : 1-dicarboxylic acid becomes black merely when kept in some samples of cold toluene. The acids were all soluble in water, the higher ones forming gels in concentrated aqueous solution, and the two lowest acids were hygroscopic.

1-*Chloroalkane*-1-*carboxylic acids.* Decarboxylation of the dibasic acids was brought about by heating them at 120—130° for about 1 hour. The products were clean and colourless and of constant b. p. The yields were practically quantitative. The acids had smells similar to those of the corresponding unsubstituted acids, but much fainter. When rubbed on the skin, they caused a delayed burning sensation. Except for the first member they were insoluble in water.

Ethyl esters of 1-*chloroalkane*-1-*carboxylic acids.* These esters were prepared in the usual way by the Fischer–Speier method, the reaction time in all cases being 3 hours. The yields rose steadily from 61% in the case of the lowest member to 97% with the highest.

Derivatives. Despite repeated recrystallisation the anilides of the 1-chloroalkane-1-carboxylic acids failed to give sharp m. p.s. The amides were prepared from the acid chlorides in the usual way, giving clean colourless initial products which on recrystallisation were obtained as white plates of sharp m. p.

The authors are indebted to the Travis Research Trust for the gift of certain chemicals, and to Dr. T. S. Ma for performing the microanalytical determinations of carbon, hydrogen, and nitrogen.—Victoria University College, Wellington, New Zealand; and University of Otago, Dunedin, New Zealand. [*Received, February* 16*th*, 1950.]

Preparation of Some Derivatives of p-*Hydroxybenzamidine.* By M. W. Partridge.

Interest in derivatives of *p*-hydroxybenzamidine arose from the high activity against *Mycobacterium tuberculosis in vitro* exhibited by certain di-(*p*-*N*-arylamidinophenoxy)alkanes, *p*-alkoxy-*N*-arylbenzamidines (Partridge, *J.*, 1949, 2683, 3043), and *p*-(ω-alkoxyalkoxy)-*N*-arylbenzamidines (Cooper and Partridge, *J.*, 1950, 459). The *N*-substituted amidines were obtained from *p*-cyanophenol by standard methods (Oxley and Short, *J.*, 1946, 147; Partridge and Short, *J.*, 1947, 390). Nitration, bromination, and iodination of *p*-hydroxybenzamidine were employed for the preparation of the corresponding nitro-, dibromo-, and di-iodo-derivatives; hydrolysis of these compounds to the known substituted benzoic acids demonstrated that substitution occurred in the positions *ortho* to the hydroxyl group. Reduction of 3-nitro-4-hydroxybenzamidine afforded 3-amino-4-hydroxybenzamidine.

Biological Results.—The method of testing was that previously described (Partridge, *J.*, 1949, 2683). Apart from *p*-hydroxy-*NN*-diphenylbenzamidine and 3-amino-4-hydroxybenzamidine which inhibited the growth of *M. tuberculosis* at dilutions of 1 : 5000, none of the amidines described here was active at a dilution of 1 : 1000. The absence of activity in *p*-hydroxy-*N*-phenylbenzamidine is of interest since the corresponding *p*-alkoxy-*N*-phenylbenzamidines are active *in vitro*, at dilutions of up to 1 : 5,000,000 in the case of the *p*-hexyloxy-homologue.

Experimental.—p-*Hydroxy*-*N*-*phenylbenzamidine.* *p*-Cyanophenol (11·9 g.) and anilinium benzenesulphonate (25·1 g., 1 mol.), when heated together at 210° for 1 hour, reacted exothermally. Crystallisation of the cooled melt from aqueous ethanol afforded p-*hydroxy*-*N*-*phenylbenzamidinium benzenesulphonate* (22 g., 66%), m. p. 183—184° (Found: N, 7·7. $C_{19}H_{18}O_4N_2S$ requires N, 7·6%).

p-*Hydroxy*-*NN*-*diphenylbenzamidine.* Diphenylamine (8·45 g.) was gradually added to molten anhydrous benzenesulphonic acid (7·9 g., 1 mol.); *p*-cyanophenol (6 g., 1 mol.) was added and the mixture was heated at 210° for 90 minutes. The cooled melt on crystallisation from aqueous ethanol yielded the *amidinium benzenesulphonate* (10·1 g., 45%) as leaflets, m. p. 263—264° (decomp.) (Found:

N, 6·3. $C_{13}H_{12}O_4N_2S$ requires N, 6·3%). The ***base***, precipitated by ammonia from an aqueous ethanolic solution of the foregoing salt, crystallised from ethanol with solvent of crystallisation and had m. p. 102—104° (decomp.); from ethyl acetate, it separated as prisms, m. p. 200—202° (Found: N, 9·7. $C_{13}H_{11}ON_3$ requires N, 9·9%); the ***hydrochloride***, prisms from methanol–acetone, had m. p. 256—257° (decomp.) (Found: N, 8·9. $C_{13}H_{11}ON_3Cl$ requires N, 8·7%); the ***picrate*** had m. p. 252—253° (Found: N, 13·5. $C_{19}H_{14}O_8N_6$ requires N, 13·6%).

p-*Hydroxy*-N-p′-*nitrophenylbenzamidine* was obtained as its ***benzenesulphonate*** by heating *p*-cyanophenol (5·95 g.) and *p*-nitroanilinium benzenesulphonate (14·8 g., 1 mol.) at 190° for 75 minutes and crystallising the product from water; the yield was 14·8 g. (71%), and the m. p. 262—264° (decomp.) (Found: N, 10·15. $C_{19}H_{17}O_6N_3S$ requires N, 10·1%).

p-*Hydroxy*-N-*methylbenzamidine*. The product obtained by heating together *p*-cyanophenol (11·9 g.) and methylammonium thiocyanate (9 g., 1 mol.) for 3 hours at 180° was dissolved in hot water (10 c.c.) and poured into aqueous ammonia (*d* 0·880; 20 c.c.); p-***hydroxy*-N-*methylbenzamidine dihydrate*** (10·8 g., 53%), which separated, was obtained as needles (from water), m. p. 260—261° (decomp.) (Found: N, 13·9, 13·8. $C_8H_{10}ON_2,2H_2O$ requires N, 13·85%). The ***nitrate***, m. p. 170—171° (decomp.), crystallised as needles from water (Found: N, 19·5. $C_8H_{11}O_4N_3$ requires N, 19·7%); the ***picrate***, crystallised from aqueous methanol, had m. p. 217—218° (decomp.) (Found: N, 18·6. $C_{14}H_{13}O_8N_5$ requires N, 18·5%).

3-*Nitro*-4-*hydroxybenzamidine*. Finely powdered *p*-hydroxybenzamidinium nitrate (2 g.) (Partridge and Short, *loc. cit.*), added during 15 mins. to ice-cold concentrated sulphuric acid (4 c.c.), was kept at 0° for 30 minutes and at 20° for 90 minutes. Material, precipitated at 0° by the addition of aqueous ammonia, afforded, on neutralisation to Congo-red with aqueous benzenesulphonic acid and crystallisation from water, 3-*nitro*-4-*hydroxybenzamidinium benzenesulphonate* (1·9 g., 56%) as pale brown prisms, m. p. 162° (Found: N, 12·6. $C_{13}H_{13}O_6N_3S$ requires N, 12·4%). A further quantity was obtained from the mother-liquors as the ***picrate*** (1·1 g., 35%), needles (from aqueous 2-ethoxyethanol), m. p. 258—260° (decomp.) (Found: N, 20·6. $C_{13}H_{10}O_{10}N_6$ requires N, 20·5%). Only unchanged *p*-hydroxybenzamidine was recovered in attempts to carry out this nitration in glacial acetic acid.

Hydrolysis of this amidine by boiling with 2*N*-sodium hydroxide for 90 minutes gave a 92% yield of 3-nitro-4-hydroxybenzoic acid, m. p. 184—185°, not depressed on admixture with an authentic specimen (Griess, *Ber.*, 1887, **20**, 408).

3 : 5-*Dibromo*-4-*hydroxybenzamidine*. *p*-Hydroxybenzamidine dihydrate (1 g.), suspended in water (10 c.c.) and neutralised to Congo-red with aqueous hydrobromic acid, was treated at 0°, during 10 minutes, with bromine (2·5 g. dissolved in 25 c.c. of 15% aqueous potassium bromide; 2·7 mols.) and kept at 20° for 30 minutes. The precipitate (1·75 g., 80%), m. p. 290—292° (decomp.), afforded pure 3 : 5-*dibromo*-4-*hydroxybenzamidinium bromide*, as needles, m. p. 293—294° (decomp.), from *N*-hydrobromic acid (Found: N, 7·5; Br, 63·5. $C_7H_8ON_2Br_2,HBr$ requires N, 7·5; Br, 64·0%). The *picrate*, m. p. 312—314° (decomp.), crystallised from aqueous 2-ethoxyethanol (Found: N, 13·1. $C_{13}H_9O_8N_5Br_2$ requires N, 13·4%). Hydrolysis of the foregoing amidine by boiling 2*N*-sodium hydroxide afforded 3 : 5-dibromo-4-hydroxybenzoic acid, m. p. 267—268° (decomp.), not depressed on admixture with the compound prepared according to Robertson (*J.*, 1902, **81**, 1482).

3 : 5-*Di-iodo*-4-*hydroxybenzamidine*. *p*-Hydroxybenzamidine dihydrate (5·16 g.), dissolved in 5*N*-sulphuric acid (13 c.c., 1·1 mols.) at 60°, was treated during 90 minutes with a solution of potassium iodide (3·32 g., 0·66 mol.) and potassium iodate (3·21 g., 0·5 mol.) in water (80 c.c.). The precipitate, on crystallisation from aqueous benzenesulphonic acid, afforded 3 : 5-*di-iodo*-4-*hydroxybenzamidinium benzenesulphonate* (5·3 g., 57%) which after recrystallisation from ethanol–*n*-butanol had m. p. 240—241° (decomp.), iodine being evolved at 236° (Found: N, 5·25; I, 46·2. $C_{13}H_{10}O_6N_2I_2S$ requires N, 5·15; I, 46·5%). *p*-Hydroxybenzamidine (40%) was recovered from the mother-liquors from the iodination.

3 : 5-Di-iodo-4-hydroxybenzoic acid (96%) was obtained on hydrolysis of the foregoing amidine by boiling 2*N*-sodium hydroxide. The m. p. of this acid, 248—249° (decomp.) (cf. Henry and Sharp, *J.*, 1922, **121**, 1059), was undepressed by the authentic compound (*Org. Synth.*, 1934, **14**, 53).

3-*Amino*-4-*hydroxybenzamidine*. 3-Nitro-4-hydroxybenzamidine (5·5 g.) was refluxed for 1 hour with stannous chloride (22 g., 3·6 mols.), concentrated hydrochloric acid (36 c.c.), and tin (12·3 g., 3·4 mols.), and the liquid was filtered and partly neutralised with aqueous ammonia. After removal of tin by hydrogen sulphide, the dihydrochloride was salted out with concentrated hydrochloric acid; the yield was 4 g. (51%), and the m. p. 290° (decomp.); Andrewes, King, and Walker (*Proc. Roy. Soc., B*, 1946, **133**, 30) record m. p. 292° (efferv.). The mother-liquors, after neutralisation, afforded the ***dipicrate*** (2·6 g., 14%), which crystallised as needles (from water), m. p. 210—212° (decomp.) (Found: N, 20·5. $C_{19}H_{16}O_{15}N_8$ requires N, 20·7%).

Reduction with zinc dust in neutral solution gave a 48% yield of the amino-amidine, identified as the dipicrate and as the neutral ***sulphate***, which formed colourless needles, m. p. 266—267° (decomp.), on crystallisation from dilute sulphuric acid (Found: N, 16·6. $C_7H_9ON_3,H_2SO_4$ requires N, 16·85%). Iron-reduction afforded 53% of the amino-amidine which was characterised as the dipicrate and neutral sulphate.

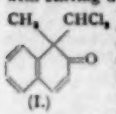
NN′-*Di*-p-***hydroxyphenylformamidine***. Ethyl orthoformate (14·8 g.) and *p*-aminophenol (21·8 g., 2 mols.) were heated together at 100° for 1 hour. Crystallisation of the resulting resin from isopropanol afforded the ***formamidine*** (7·2 g., 25%) which melted with effervescence at 120—130°, solidified, and again melted at 188—189° (decomp.) (Found: N, 9·7. $C_{13}H_{12}O_2N_2,C_3H_6O$ requires N, 9·7%). The ***hydrochloride***, which crystallised as needles from dilute hydrochloric acid, sintered at 105—110°, began to decompose at 207°, and melted at 237—238° (Found: N, 9·4. $C_{13}H_{12}O_2N_2,HCl,2H_2O$ requires N, 9·3%).

The author gratefully acknowledges his indebtedness to Mr. C. E. Coulthard, Dr. L. Dickinson, and Miss B. Croshaw for the biological tests.—RESEARCH LABORATORIES, MESSRS. BOOTS PURE DRUG CO., LTD., NOTTINGHAM. UNIVERSITY OF NOTTINGHAM. [*Received, March 8th*, 1950.]

The Reactivity of β-Naphthols and β-Naphthylamines. By. F. Bell and W. H. Hunter.

Many papers have dealt with the low reactivity of the 3-position in β-naphthols and β-naphthylamines and the following experiments still further exemplify this point.

Reimer–Tiemann Reaction with 1-Methyl-2-naphthol.—1-Methyl-2-naphthol (10 g.; Robinson and Weygand, *J.*, 1941, 387) was added to sodium hydroxide (18·2 g.) dissolved in water (38 c.c.) and ethanol (30 c.c.). The mixture was heated to 70° on the water-bath, and chloroform (11·5 g.) added dropwise with stirring during 30 minutes. The stirring was continued for 1 hour, and the contents of the flask were cooled and made acid with concentrated hydrochloric acid (*ca.* 20 c.c.). The dark oil which separated was extracted with ether, dried, and distilled *in vacuo*, yielding 9·7 g. of a pale yellow oil, b.p. 130—132°/2 mm. The oil solidified when kept for several days, yielding prisms of *2-keto-1-methyl-1-dichloromethyl-1 : 2-dihydronaphthalene* (I), m.p. 65°, more expeditiously obtained by vigorous scratching of the oil with 50% alcohol (Found : C, 59·8; H, 4·0. $C_{12}H_{10}OCl_2$ requires C, 59·8; H, 4·1%). The ketone did not yield an oxime, semicarbazone, or phenylhydrazone.



(I.)

Reimer–Tiemann Reaction with 1-Ethyl-2-naphthol.—1-Ethyl-2-naphthol was prepared in 38% yield by Clemmensen reduction of 1-acetyl-2-naphthol in toluene (cf. Imoto, *J. Chem. Soc. Japan*, 1937, **58**, 932). In the Reimer–Tiemann reaction it yielded an oil, b.p. 140—142°/0·2 mm., which was similar to the above but did not solidify and could not be obtained pure.

Attempted Coupling of 1-Methyl-2-naphthol with Diazotised Picramide.—1-Methyl-2-naphthol in glacial acetic acid was added to diazotised picramide (Misslin, *Helv. Chem. Acta*, 1920, **3**, 626) at 0° to −3°. Stirring was continued for 1 hour, and the mixture poured on ice, but essentially unchanged 1-methyl-2-naphthol was precipitated.

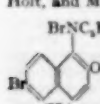
Nitration of 1-Bromo-2-toluene-p-sulphonamidonaphthalene in Pyridine (method of Battegay and Brandt, *Bull. Soc. chim.*, 1922, **31**, 910).—Freshly distilled nitrobenzene (120 c.c.) and pyridine (75 c.c.) were mixed and cooled to 0°, and nitric acid (7·5 c.c.; *d* 1·51) added. Nitrogen peroxide was removed by a current of air, and 1-bromo-2-toluene-*p*-sulphonamidonaphthalene (37 g.) added. The solution was heated in an oil-bath at 60° for 2 hours and then to 120° for 2 hours, considerable quantities of nitrogen peroxide then being evolved. The cooled mixture was poured into water and made alkaline, and the nitrobenzene removed in steam. The residual yellow liquid was decanted from a little tar and made acid. 1-Bromo-6-nitro-2-toluene-*p*-sulphonamidonaphthalene (34 g.) was precipitated (m. p. 195° alone or mixed with an authentic sample).

1-Bromo-2-N-methylnaphthylamine.—To 2-N-methylnaphthylamine (Pschorr and Karo, *Ber.*, 1906, **39**, 3141) (50 g.) in chloroform (500 c.c.), cooled in ice, bromine (51 g.) in chloroform (50 c.c.) was slowly added. The mixture was left overnight, and the hydrobromide of 1-bromo-2-*N*-methylnaphthylamine (56 g.) separated. This was decomposed by 10% ammonia solution, and the liberated oil shaken until solid. *1-Bromo-2-N-methylnaphthylamine* crystallised from methanol, ethanol, or light petroleum in white leaflets, m. p. 46° (34 g.) (Found : C, 56·1; H, 4·2. $C_{11}H_{10}NBr$ requires C, 56·0; H, 4·2%). The *hydrochloride*, precipitated from ether solution by hydrogen chloride, formed white needles, m. p. 178° (decomp.) decomposed by water (Found : equiv., 277. $C_{11}H_{10}NBr,HCl$ requires equiv., 273); the *benzoyl* derivative, formed white needles, m. p. 111°, from ethanol (Found : C, 63·6; H, 4·6. $C_{18}H_{14}ONBr$ requires C, 63·7; H, 4·2%).

1-Bromo-N-nitroso-2-N-methylnaphthylamine.—Sodium nitrite solution (30 c.c.; 10%) was slowly added to a vigorously stirred solution of the amine (10 g.) in hydrochloric acid (6 c.c. in 150 c.c. of water). The precipitated red solid on recrystallisation from 60% ethanol gave the *nitroso*-compound as pinkish leaflets, m. p. 119—120° (8·4 g., 80%) (Found : C, 50·1; H, 3·6. $C_{11}H_9ON_2Br$ requires C, 49·8; H, 3·4%).

Attempts to cause Migration of the Nitroso-group in 1-Bromo-N-nitroso-2-N-methylnaphthylamine.—(*a*) The nitrosoamine (2 g.) was suspended in absolute alcohol (10 c.c.), and saturated absolute alcoholic hydrogen chloride (10 c.c.) added at −5° with stirring. After being left for 4 days at −5°, the nitrosoamine was recovered unchanged in 75% yield, and no basic material could be isolated. (*b*) Repetition of this procedure, sufficient alcohol being used for dissolution, resulted only in formation of 1-bromo-2-*N*-methylnaphthylamine. With glacial acetic acid as solvent the same result was obtained.

3-Chloro-2-naphthol.—3-Chloro-2-naphthol is stated to have m. p. 63—64·5° when prepared from 3-hydroxy-2-naphthoic acid *via* 3-chloro-2-methoxynaphthalene (Jambuserwala, Holt, and Mason, *J.*, 1931, 374), whereas prepared by chlorination of α-nitroso-β-naphthol it has m. p. 90° (Marschalk, *Bull. Soc. chim.*, 1928, **43**, 1361). Marschalk's result is now confirmed. 3-Chloro-2-methoxynaphthalene, prepared from Marschalk's 3-chloro-2-naphthol, proved identical with that obtained by Jambuserwala, Holt, and Mason's method. Demethylation of the methoxy-compound by hydriodic acid did not proceed smoothly and mixtures were obtained from which a pure phenol could not be isolated. This difficulty in demethylating 3-substituted 2-naphthyl ethers has been reported also by Clemo and Spence (*J.*, 1928, 2819). The correct m. p. of 3-chloro-2-naphthol is, therefore, 90°, and Marschalk's experiment provides one of the few examples of group entry in position 3.



(II.)

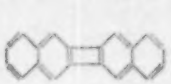
Bromination of 1-Bromo-2-naphthol in Pyridine.—This led only to the isolation of (II), previously obtained by Fries and Schimmelschmidt (*Annalen*, 1930, **484**, 245) from the interaction of 1 : 1-dibromo-2-keto-1 : 2-dihydronaphthalene with pyridine. Similar high-melting, nitrogen-containing compounds were obtained by interaction of both 1-methyl-2-naphthol and 2 : 2′-dihydroxy-1 : 1′-dinaphthyl with bromine in pyridine.

One of the authors (W. H. H.) gratefully acknowledges the receipt of a grant from the Department of Scientific and Industrial Research.—College of Technology, Belfast. [*Received, May 22nd*, 1950.]

Dinaphthylenes. By F. Bell and W. H. Hunter.

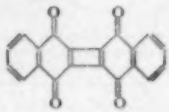
Although o-diphenylene (I) has been the subject of much study on account of the *cyclo*butadiene system which it contains, the closely related dinaphthylenes (II and isomers) have been comparatively neglected. Von Braun and Kirschbaum (*Ber.*, 1921, **54**, 597) obtained from 1 : 2-dihydronaphthalene with sulphuric acid a bisdialin which on distillation with lead oxide gave a yellow powder, m. p. 165°, of composition $C_{20}H_{12}$. The same compound can be obtained by the selenium dehydrogenation of the hydrocarbon, $C_{20}H_{16}$, obtained by interaction of tetralin with aluminium chloride (Dansi and Ferri, *Gazzetta*, 1941, **71**, 645; Dansi and Reggiani, *ibid.*, 1948, **78**, 801). Orchin and Reggel (*J. Amer. Chem. Soc.*, 1947, **69**, 505) by pyrolysis of 1 : 2′-dinaphthyl obtained a mixture of two benzfluoranthenes, one, m. p. 166°, apparently identical with the above material, and the other, m. p. 217°, identical with 11 : 12-benzfluoranthene synthesised from acenaphthenequinone by Mouren (*Bull. Soc. chim.*, 1948, **15**, 99). It appears therefore that the hydrocarbon, $C_{20}H_{12}$, is a 10 : 11-benzfluoranthene (III) and not a dinaphthylene.

(I.)



(II.)

(III.)



(IV.)

Rosenhauer, Braun, Pummerer, and Riegelbauer (*Ber.*, 1937, **70**, 2281) obtained from α-naphthaquinone a compound to which they assigned the structure (IV), and from this, by distillation with zinc dust, a hydrocarbon, m. p. 365°, to which the formula (II) was ascribed. Although it is easy to obtain (IV), we have failed to convert it into a hydrocarbon by distillation with zinc dust under various conditions.

The most direct route to the dinaphthylenes appeared to be the linking of two molecules of a 1 : 2- or 2 : 3-dibromonaphthalene by the Ullmann or the Grignard–cupric chloride reaction. However, the only product from the Ullmann reaction was an uncrystallisable tar, whilst the interaction of both atoms of a dibromonaphthalene with magnesium could not be realised, one half of the magnesium being unattacked. A similar failure to prepare a Grignard compound from *p*-dibromobenzene was reported by Fink (*J.*, 1923, **123**, 3418).

The interaction of 1 : 2-dibromonaphthalene with naphthalene under the influence of aluminium chloride or of 1 : 2- and 2 : 3-dibromonaphthalenes with sodium or potassium yielded no useful result.

The attempted twofold linking of naphthalene derivatives having met with no success, the formation of a second linkage between the two nuclei of a dinaphthyl was attempted. Ring closure of 1-bromo-2 : 2′-dinaphthyl by means of aluminium chloride in various solvents and the reaction of 1 : 1′-dibromo-2 : 2′-dinaphthyl with copper and with sodium were investigated without result.

The Pschorr reaction on diazotised 1-amino-2 : 2′-dinaphthyl appeared a possible route. The base has been described by Cumming and Howie (*J.*, 1933, 532) but repetition of their experiment gave only 1 : 2 : 7 : 8-dibenzcarbazole, previously prepared by Vesely (*Ber.*, 1905, **38**, 139) by reduction of 1 : 1′-dinitro-2 : 2′-dinaphthyl (cf. Huisberg and Sorge, *Annalen*, 1950, **566**, 162). Variations of the reduction method (tin, stannous chloride, aluminium amalgam) yielded the carbazole, as with zinc dust, but on prolonging the original zinc dust reduction elimination of the nitro-group took place and 2 : 2′-dinaphthyl was obtained.

1-*Bromo*-2 : 2′-*dinaphthyl*.—2 : 2′-Dinaphthyl (10 g.) and *N*-bromosuccinimide (7·5 g.) were refluxed for 8 hours in dry chloroform (200 c.c.). The mixture, after filtration from succinimide, was evaporated, and the residue crystallised from ethanol, giving needles, m. p. 123° (Found: C, 72·2; H, 3·9. $C_{20}H_{13}Br$ requires C, 72·5; H, 3·9%). Monobromination could not be achieved directly.

1-*Nitro*-2 : 2′-*dinaphthyl*.—2 : 2′-Dinaphthyl (10 g.) was dissolved in acetic acid (180 c.c.) and quickly cooled. Nitric acid (6 c.c.; *d* 1·52) was added, and the mixture heated on a steam-bath for 2 hours. The crystals of 2 : 2′-dinaphthyl gradually disappeared, giving a yellow solution which deposited yellow needles on cooling. Recrystallisation from acetic acid gave 1-nitro-2 : 2′-dinaphthyl (8·4 g.), m. p. 179°. The directions of Cumming and Howie (*J.*, 1931, 3180) led to a negligible yield of this nitro-compound.

We believe that a true dinaphthylene has still to be described.—College of Technology, Belfast. [*Received, May 24th*, 1950.]

2- *and* 4-*Nitro*-3-*aminocarbazole*. By George Anderson and Neil Campbell.

Kehrman and Zweifel (*Helv. Chim. Acta*, 1928, **11**, 1213) by nitration of the diacetyl and triacetyl derivatives of 3-aminocarbazole obtained products which on hydrolysis gave two isomers, m. p. 233° and 177°, and were termed α- and β-nitro-3-aminocarbazole, respectively. We have now shown that the α-compound is the 2-nitro-compound since it yielded by the diazo-reaction 2-nitrocarbazole identical with an authentic sample prepared from 7-nitro-1 : 2 : 3 : 4-tetrahydrocarbazole (Barclay and Campbell, *J.*, 1945, 530). The β-compound is therefore 4-nitro-3-aminocarbazole. On this basis the following m. p.s may be assigned. 2-Nitro-3-diacetylamino-, m. p. 226°, 2-nitro-3-acetamido-, m. p. 275°, 4-nitro-3-acetamidocarbazole, m. p. 198°.

Information on 2-aminocarbazole is scanty and incomplete. Blank (*Ber.*, 1891, **24**, 306) by the pyrolysis of "diphenylin," presumably 2 : 4′-diaminodiphenyl, obtained a product, m. p. 238°, which he considered to be 2-aminocarbazole but for which he did not record an analysis. King and King

(*J.*, 1945, 824) obtained a product, m. p. 240°, from 3-acetamidobenzocinnoline, which they believed to be 2-aminocarbazole. It has been claimed that the compound is obtained by heating 2 : 2' : 4'-triaminodiphenyl-4-sulphonic acid with dilute acid followed by removal of the sulphonic group (G.P. 542,422), but no m. p. or analysis was given. It was therefore decided to repeat Blank's work, and the product obtained was found to be identical with 2-aminocarbazole obtained by the reduction of 2-nitrocarbazole (Barclay and Campbell, *loc. cit.*).

Experimental.—Nitration of acetylated 3-aminocarbazole. Reduction of 3-nitro- to 3-amino-carbazole was best effected by hydrogenation in ethanol with Adams's platinum catalyst. Reduction with stannous chloride–hydrochloric acid (Kehrmann and Zweifel, *loc. cit.*) or ethanolic potassium hydroxide (Whitner, *J. Amer. Chem. Soc.*, 1924, **46**, 2326) gave yields of 25 and 80%, respectively. Excess of acetic anhydride was added to 3-aminocarbazole (5 g.) dissolved in acetic acid, and after several hours the mixture was poured into water. 3-Acetamidocarbazole separated and crystallised from ethanol, formed prisms, m. p. 215° (3·5 g.). 3-Acetamidocarbazole (10 g.) was boiled with acetic anhydride (50 ml.) and sulphuric acid (0·5 ml.) for 45 minutes and then poured into water; the resulting solid was purified by extraction with benzene. Evaporation of the solvent gave a mixture of diacetyl- and triacetyl-3-aminocarbazole as a yellow crystalline solid (11 g.), m. p. 145—165°. Nitration of this mixture was effected by Kehrmann and Zweifel's method (*loc. cit.*). 2-Nitro-3-diacetylaminocarbazole, m. p. 226°, separated first, followed by a mixture of 2-nitro- and 4-nitro-3-diacetylaminocarbazole. This mixture (4 g.) was ground with concentrated ethanolic sodium hydroxide until, on addition of a drop of the mixture to water, no yellow solid resulted. The mixture on filtration gave a filtrate (*A*) and 2-nitro-3-acetamidocarbazole as red needles, m. p. 275°, which when heated with ethanol–hydrochloric acid (equal volumes) followed by treatment with ammonia gave 2-nitro-3-aminocarbazole (1·6 g.), violet needles (from ethanol), m. p. 233°. Attempts to isolate 4-nitro-3-acetamidocarbazole from the filtrate (*A*) were only partly successful (cf. Kehrmann and Zweifel, *loc. cit.*). Chromatographic separation was complicated by hydrolysis of the acetyl compounds on the column. The best separation was effected by grinding the mixture of nitro-compounds (5 g.) for 15 minutes with concentrated sodium hydroxide, filtering off the 2-nitro-3-acetamidocarbazole, and pouring the filtrate into water. Filtration gave a filtrate (*B*) and a residue which crystallised from ethanol in yellow elongated prisms, m. p. 224°, depressed on admixture with 2-nitro-3-diacetylaminocarbazole. It was assumed to be *4-nitro-3-diacetylaminocarbazole* (Found: C, 61·7; H, 3·9. $C_{16}H_{13}O_4N_3$ requires C, 61·7; H, 4·2%). Reduction of the volume of the filtrate (*B*) gave 4-nitro-3-acetamidocarbazole, which crystallised from ethanol in brown needles (1·5 g.), m. p. 198°. Hydrolysis with ethanol–hydrochloric acid yielded 4-nitro-3-aminocarbazole, deep red needles, m. p. 175—177° (lit., 177°).

2- and 4-Nitrocarbazoles. 2-Nitro-3-aminocarbazole, m. p. 233° (0·2 g.), was dissolved in boiling ethanol and 0·3 g. of 20% ethanolic sulphuric acid was added. Diazotisation at 0° with sodium nitrite (0·08 g.) in water (0·14 g.) gave a clear solution which was boiled for 30 minutes and evaporated to a small volume. Addition of water to the hot solution until it was turbid, and cooling gave 2-nitrocarbazole, yellow needles (from benzene, charcoal), m. p. 173°, giving no depression when mixed with an authentic sample and a 20° depression with 4-nitrocarbazole. 4-Nitro-3-aminocarbazole likewise yielded 4-nitrocarbazole, which after chromatographic purification on alumina followed by sublimation was obtained in small yield as yellowish-orange plates, m. p. 179—180°, undepressed when mixed with an authentic sample.

2-Aminocarbazole. (*a*) 2-Nitrocarbazole (0·2 g.) in ethanol (100 ml.) was quickly hydrogenated at 60 lb. pressure with Adams's platinum catalyst. Evaporation of part of the solvent gave 2-aminocarbazole, which crystallised as unstable colourless needles (0·04 g.), m. p. 238—239° (Found: C, 78·3; H, 5·7; N, 14·9. Calc. for $C_{12}H_{10}N_2$: C, 78·1; H, 5·5; N, 15·4%). It gave characteristic colours with mixtures of nitric and sulphuric acids, or sulphuric and selenious acids. 3- and 4-Nitrocarbazoles similarly yielded 3- and 4-aminocarbazoles, but the latter could not be purified. It gave with acetyl chloride and pyridine the *acetyl* derivative, obtained after chromatography on alumina and crystallisation from light petroleum as colourless needles, m. p. 183—185° (Found: C, 75·3; H, 6·0; N, 12·3. $C_{14}H_{12}ON_2$ requires C, 75·0; H, 5·4; N, 12·5%).

(*b*) 2 : 4'-Dinitrodiphenyl (5 g.) was hydrogenated in ethanol (300 ml.) with Adams's platinum catalyst (0·1 g.) at 60 lb. pressure. Removal of the solvent gave 2 : 4'-diaminodiphenyl as an oil which was mixed with lime and pyrolysed in a glass tube 18 in. long, packed loosely with lime and heated to redness. A brown liquid was obtained which crystallised first from ethanol, then from benzene–light petroleum in colourless needles, m. p. 238° alone or admixed with 2-aminocarbazole prepared as above (Found: C, 79·1; H, 5·6; N, 15·0).—University of Edinburgh. [*Received, June 13th*, 1950.]

Sulphanilyl Derivatives of 2-Amino-3 : 6-di-sec.-butylpyrazine. By G. T. Newbold.

In connection with investigations on the structure of aspergillic acid (see Dunn, Gallagher, Newbold, and Spring, *J.*, 1949, S126, for summary) a method for the synthesis of 2-amino-3 : 6-di-*sec.*-butylpyrazine was developed (Newbold and Spring, *J.*, 1947, 373). Starting from this latter compound the preparation of 3 : 6-di-*sec.*-butyl-2-sulphanilamido- (I), 3 : 6-di-*sec.*-butyl-2-N^4-(hydrogen succinoyl)sulphanilamido- (II), and 3 : 6-di-*sec.*-butyl-2-N^4-(hydrogen phthaloyl)sulphanilamido-pyrazine (III) is described. Some *in vitro* antibacterial tests on these compounds are reported in the Table.

Minimal inhibitory conen. in mg. per 100 c.c. of medium.

	Strep. haem.:		*Staph aureus:*	*B. coli:*	
Compound.	broth.	blood.	broth.	broth.	synthetic.
(I)	2	>2	>5	>5	>5
(II)	5	>2	>5	>5	>5
(III)	>2	—	>2	>2	>2

Experimental.—2-N^4-*Acetylsulphanilamido*-3 : 6-*di*-sec.-*butylpyrazine*. Acetylsulphanilyl chloride (1·05 g.) was added in small portions to a cooled solution of 2-amino-3 : 6-di-*sec.*-butylpyrazine (0·9 g.) in dry pyridine (2 c.c.). The reaction mixture was heated on the water-bath for 1 hour, cooled, and poured into water (20 c.c.). The reaction product was collected and crystallised from aqueous ethanol from which 2-N^4-*acetylsulphanilamido*-3 : 6-*di*-sec.-*butylpyrazine* (1·1 g.) separated as needles, m. p. 187—189° (Found : C, 59·9; H, 6·8; N, 14·1. $C_{20}H_{26}O_3N_4S$ requires C, 59·4; H, 6·9; N, 13·9%).

3 : 6-*Di*-sec.-*butyl*-2-*sulphanilamidopyrazine*. The acetyl compound (0·5 g.), dissolved in a mixture of hydrochloric acid (*d* 1·19; 10 c.c.) and ethanol (50%; 10 c.c.), was heated on the water-bath for 1½ hours. The reaction mixture from which a crystalline solid had separated was cooled and filtered. The filtrate was evaporated to dryness under reduced pressure and the residue combined with the crystalline solid and dissolved in dilute aqueous alkali, the solution then being made just acid with acetic acid. The precipitated 3 : 6-*di*-sec.-*butyl*-2-*sulphanilamidopyrazine* (0·40 g.) crystallised from aqueous ethanol as needles, m. p. 161° (Found : C, 59·9; H, 7·2; N, 13·3. $C_{18}H_{26}O_2N_4S$ requires C, 59·7; H, 7·2; N, 15·5%).

3 : 6-*Di*-sec.-*butyl*-2-p-*succinimidobenzenesulphonamidopyrazine*. 2-Amino-3 : 6-di-*sec.*-butylpyrazine (1·0 g.) in dry pyridine (5 c.c.) was treated with *p*-succinimidobenzenesulphonyl chloride (1·35 g.; Adams, Long, and Jeans, *J. Amer. Chem. Soc.*, 1939, **61**, 2346; Moore and Miller, *ibid.*, 1942, **64**, 1572; Picard, Reid, and Seymour, *J.*, 1946, 751) added during 15 minutes, and the reaction mixture heated on the water-bath for 1 hour. The dark reaction mixture was treated with ice-water; the oily product solidified on storage. The solid was thrice crystallised from ethanol (charcoal), giving 3 : 6-*di*-sec.-*butyl*-2-p-*succinimidobenzenesulphonamidopyrazine* (1·0 g.) as blades, m. p. 179—181° (Found : C, 59·1; H, 6·6; N, 12·8. $C_{22}H_{28}O_4N_5S$ requires C, 59·5; H, 6·3; N, 12·6%).

3 : 6-*Di*-sec.-*butyl*-2-*sulphanilamidopyrazine from* 3 : 6-*di*-sec.-*butyl*-2-p-*succinimidobenzenesulphonamidopyrazine*. The compound (100 mg.) in ethanol (1 c.c.), hydrochloric acid (*d* 1·19; 2 c.c.), and water (1 c.c.) was heated on the water-bath for 75 minutes. The solution was cooled, made just acid with dilute acetic acid, and after some time the precipitate was collected. Crystallisation from aqueous ethanol gave needles (60 mg.), m. p. 161° alone or when admixed with 3 : 6-di-*sec.*-butyl-2-sulphanilamidopyrazine.

3 : 6-*Di*-sec.-*butyl*-2-N^4-(*hydrogen succinoyl*)*sulphanilamidopyrazine*. (*a*) The succinimido-compound (0·5 g.) was heated under reflux for 2 hours with sodium hydroxide solution (2N.; 5 c.c.), water (20 c.c.), and ethanol (25 c.c.). The solution was concentrated under reduced pressure to small bulk and acidified with acetic acid, and the precipitate collected. Three crystallisations from aqueous ethanol gave 3 : 6-*di*-sec.-*butyl*-2-N^4-(*hydrogen succinoyl*)*sulphanilamidopyrazine* (0·45 g.) as felted needles, m. p. 200° (Found : C, 57·4; H, 6·1; N, 11·8. $C_{22}H_{30}O_5N_4S$ requires C, 57·1; H, 6·5; N, 12·1%).

(*b*) Succinylsulphanilyl chloride (0·65 g.; Picard, Reid, and Seymour, *loc. cit.*) was added in portions with shaking to an ice-cooled solution of 2-amino-3 : 6-di-*sec.*-butylpyrazine (0·45 g.) in dry pyridine (3 c.c.), and the mixture heated on the water-bath for 1 hour. The yellow solution was poured into ice-water (20 c.c.), the oil which separated extracted with ether (20 c.c.), and the ethereal extract (A) washed with sodium hydroxide solution (2N.; 2 c.c.). The alkaline extract was acidified with acetic acid and kept at 0°. The solid which separated was crystallised from aqueous methanol to give the hydrogen succinoyl derivative (45 mg.) as felted needles, m. p. 200° alone or when mixed with preparation (*a*) above. The ethereal solution (A) was washed with water (3 × 10 c.c.), dried (Na_2SO_4), and evaporated. The residual oil on treatment with ethanolic picric acid gave 2-amino-3 : 6-di-*sec.*-butylpyrazine picrate (0·55 g.), m. p. 131—133°, not depressed by an authentic specimen prepared after Newbold and Spring (*loc. cit.*).

(*c*) 3 : 6-Di-*sec.*-butyl-2-sulphanilamidopyrazine (250 mg.) in acetone (20 c.c.) was treated with succinic anhydride (70 mg.), and the solution refluxed for 1 hour. The acetone was removed and the residue crystallised from aqueous methanol to give the hydrogen succinoyl derivative (300 mg.) as felted needles, m. p. 200° alone or admixed with preparations (*a*) and (*b*).

3 : 6-*Di*-sec.-*butyl*-2-N^4-(*hydrogen phthaloyl*)*sulphanilamidopyrazine*. 3 : 6-Di-*sec.*-butyl-2-sulphanilamidopyrazine (250 mg.) in acetone (10 c.c.) was treated with a solution of phthalic anhydride (100 mg.) in acetone (15 c.c.) and the solution refluxed for 2 hours. The acetone was distilled off and the residue crystallised from aqueous ethanol to give 3 : 6-*di*-sec.-*butyl*-2-N^4-(*hydrogen phthaloyl*)*sulphanilamidopyrazine* as needles (320 mg.), m. p. 186—188° (Found : C, 61·0; H, 5·8; N, 11·1. $C_{26}H_{30}O_5N_4S$ requires (C, 61·2; H, 5·9; N, 11·0%).

The author is indebted to Professor F. S. Spring for his interest and encouragement and to Dr. James Walker for making the antibacterial results available.—The Royal Technical College, Glasgow. [*Received, June 15th*, 1950.]

Preparation of Benzylsuccinic Acid from Ethyl α-Methylcinnamate. By W. F. Beech and N. Legg.

Ethyl α-methylcinnamate was brominated with *N*-bromosuccinimide by the Wohl–Ziegler method. The bromo-compound reacted readily with *cyclo*hexylamine, and examination of the ultra-violet absorption spectrum ($\lambda_{max.}$ = 281 mμ.; $\varepsilon_{max.}$ = 17,000) indicated the presence of the cinnamic acid double-bond system. The compound is therefore presumably ethyl α-bromomethylcinnamate. Conversion of the bromo-ester into cyano-ester by means of cuprous cyanide did not proceed smoothly; at 100°, the bromo-ester was largely unchanged; at 200°, a tarry product was obtained from which, after hydrolysis and hydrogenation, benzylsuccinic acid was isolated in poor yield, demonstrating that the bromine atom in the bromo-ester is attached to the α-methyl group. [Ziegler *et al.* (*Annalen*, 1942, **551**, 80) obtained cinnamyl bromide by reaction of 1-phenylpropene with *N*-bromosuccinimide.]

Experimental.—Ethyl α-methylcinnamate (33 g.) (Edeleanu, *Ber.*, 1887, **20**, 617) in carbon tetrachloride (70 c.c.) was boiled under reflux with *N*-bromosuccinimide (33 g.) for 24 hours. After cooling to 20°, succinimide (19 g.) was collected and the filtrate fractionated under reduced pressure to give *ethyl α-bromomethylcinnamate* (44 g., 94%), m. p. 40—42°, b. p. 110—112°/0·03 mm. After crystallisation from ethanol, the substance had m. p. 42° (Found: C, 53·6; H, 4·85; Br, 29·45. $C_{12}H_{13}O_2Br$ requires C, 53·55; H, 4·85; Br, 29·7%).

The bromomethyl compound (18 g.) was heated with cuprous cyanide (6·2 g.) at 200° until the vigorous reaction had subsided and kept at 200° for a further 15 minutes. The resulting tar was thoroughly extracted with small amounts of hot ethanol, the united extract was clarified with carbon and poured into cold water (500 c.c.), and the resulting oil extracted with ether (120 c.c.). The ethereal solution was dried and the ether removed. After distillation under reduced pressure (2 mm.), the distillate (5·6 g.) was boiled under reflux with aqueous 2N-sodium hydroxide (100 c.c.) for 16 hours, the solution acidified and cooled, and the product collected and recrystallised from hot water. The product (1·1 g.) was dissolved in water (25 c.c.), and sodium carbonate added until the solution was faintly alkaline to litmus. After hydrogenation at room temperature and pressure in the presence of Raney nickel catalyst, the solution was filtered and acidified, giving benzylsuccinic acid, m. p. 159° (from hot water) (Fittig and Shields, *Annalen*, 1895, **285**, 207, give m. p. 160°) (Found: C, 63·5; H, 5·85. Calc. for $C_{11}H_{12}O_4$: C, 63·45; H, 5·75%).—RESEARCH LABORATORIES, IMPERIAL CHEMICAL INDUSTRIES LIMITED, BLACKLEY, MANCHESTER, 9. [*Received, July 10th*, 1950.]

A New Synthesis of Indigo. By J. HARLEY-MASON.

THIELE (*Ber.*, 1899, **32**, 1293) obtained 2-nitro-1-*o*-nitrophenylethyl alcohol (I) by condensation of *o*-nitrobenzaldehyde with nitromethane, and observed that on treatment with ferrous sulphate and alkali it gave a blue pigment, which he guessed might be indigo. We have found that (I) can be converted into indigo in high yield by treatment with alkaline sodium dithionite (hydrosulphite), or in lower yield, by other alkaline reducing agents including ammonium sulphide, zinc dust and ammonium chloride, and ferrous sulphate and sodium hydroxide.

2-Nitro-1-(4 : 5-methylenedioxy-2-nitrophenyl)ethyl alcohol (II), obtained (as sodium salt) by the condensation of 6-nitropiperonaldehyde with nitromethane in the presence of sodium methoxide, gave 5 : 6 : 5′ : 6′-bismethylenedioxyindigo on similar treatment with dithionite. The dehydration products of (I) and (II), β : 2-dinitrostyrene and β : 2-dinitro-4 : 5-methylenedioxystyrene respectively, did not thus give indigos.

Experimental.—*o*-Nitrobenzaldehyde (5 g.) and nitromethane (2·3 g.) in methanol (15 ml.) were treated slowly at 0° with a solution of sodium methoxide [from sodium (0·9 g.) and methanol (10 ml.)]. After 12 hours at 0° the yellow crystalline sodium salt of 2-nitro-1-*o*-nitrophenylethyl alcohol was collected and washed with ether. This salt (3 g.) was dissolved in water (50 ml.), 2N-sodium hydroxide (15 ml.) was added, and sodium dithionite (6·5 g.) was then added slowly with stirring. A thick precipitate of indigo was formed at once. Air was drawn through the solution for 15 minutes to oxidise any leuco-compound, and the indigo (1·51 g., 90%) collected and purified by vacuum-sublimation (Found: C, 73·0; H, 4·1; N, 10·8. Calc. for $C_{16}H_{10}O_2N_2$: C, 73·3; H, 3·8; N, 10·7%).

Similar dithionite reduction of the product from 6-nitropiperonal (4 g.) and nitromethane (1·2 g.) gave 5 : 6 : 5′ : 6′-bismethylenedioxyindigo (1·5 g., 80%) (Found: C, 61·1; H, 3·0; N, 7·9. Calc. for $C_{18}H_{10}O_6N_2$: C, 61·9; H, 2·85; N, 8·0%).—UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, July 18th*, 1950.]

Solvolysis by Bromine Trifluoride. By A. G. SHARPE.

BROMINE TRIFLUORIDE has recently been shown to be a useful reagent for the preparation of complex fluorides in a non-aqueous medium (Woolf and Emeléus, *J.*, 1949, 2865; 1950, 1050; Emeléus and Woolf, *J.*, 1950, 164; Woolf, *J.*, 1950, 1053; Emeléus and Gutmann, *J.*, 1949, 2979; 1950, 1046; Sharpe, *J.*, 1949, 2901). With its aid a number of salts unstable to water have been prepared. In the conversion of a mixture of gold and silver into silver fluoroaurate, for example, the metals are first converted into the compounds $AuBrF_4$ and $AgBrF_4$, which are respectively an acid and a base on the bromine trifluoride system; these substances then react according to the equation:

$$[BrF_2][AuF_4] + Ag[BrF_4] = Ag[AuF_4] + 2BrF_3$$

Salts prepared by such methods, however, are often impure and contain bromine; analyses of typical products indicate compositions such as $K_2SnF_6 \cdot 1{\cdot}15BrF_3$ and $NaAuF_4 \cdot 0{\cdot}1BrF_3$. The simplest explanation of this retention of the elements of bromine trifluoride, firmly combined with the salts, is solvolysis, or incomplete reaction between acid and base. Evidence for the correctness of this explanation is presented below.

Titanium tetrafluoride forms with bromine trifluoride a compound which is unstable *in vacuo* at room temperature; in solution, this reacts as $(BrF_2)_2TiF_6$, and from it nitrosyl fluorotitanate, $(NO)_2TiF_6$, may be prepared. Attempts to make metal fluorotitanates, however, lead to the formation of products heavily contaminated with bromine (Woolf, *loc. cit.*). The reversibility of the reaction

$$2KBrF_4 + (BrF_2)_2TiF_6 \rightleftharpoons K_2TiF_6 + 4BrF_3$$

has now been demonstrated by showing that (*a*) combination of acid and base is incomplete, and (*b*) bromine trifluoride effects partial decomposition of pure potassium fluorotitanate. When a mixture

of equivalent proportions of potassium bromide and titanium dioxide was treated with bromine trifluoride, and the solvent removed by evaporation *in vacuo* at room temperature, the product corresponded in composition to K_2TiF_6,0·95BrF_3, and *X*-ray powder-photographic examination revealed the presence of potassium tetrafluorobromite (bromotetrafluoride), $KBrF_4$. Pure potassium fluorotitanate, prepared from iron-free titanium dioxide, potassium fluoride, and hydrofluoric acid, dissolved readily in bromine trifluoride; removal of the solvent yielded a product, K_2TiF_6,1·1BrF_3, again shown by powder photography to have $KBrF_4$ as a principal constituent. The heavy solvolysis of the fluorotitanates, the alternative method for their preparation, the instability of the TiF_4–BrF_3 addition product, and the lower scattering power of K_2TiF_6 and TiF_4 (formed by decomposition of the TiF_4–BrF_3 compound) combine to make this instance unusually favourable for the *X*-ray powder-photographic demonstration of the presence of $KBrF_4$ in the reaction products. There is, however, no reason to doubt that the impurity of other complex salts prepared by means of bromine trifluoride has a similar origin.

Experimental.—Treatment of equivalent amounts of potassium bromide and titanium dioxide with *ca.* 3 ml. of bromine trifluoride, followed by removal of the solvent in the usual way, gave a product (I) of composition K_2TiF_6,1·1BrF_3. This was decomposed quietly by dilute sodium hydroxide solution, titanium dioxide was filtered off, and bromine was determined in the filtrate as described by Sharpe and Emeléus (*J.*, 1948, 2135) (Found: Br, 20·2%; weight equiv. to TiO_2 = 80, 390. Calc. for K_2TiF_6,1·1BrF_3: Br, 22·5%; equiv., 391).

Potassium fluorotitanate, prepared by dissolving titanium dioxide and potassium fluoride in 40% hydrofluoric acid, was recrystallised from hydrofluoric acid in a platinum vessel; its fluorine content was determined by fusion with sodium carbonate, filtration of titanium dioxide, and precipitation as calcium fluoride (Found: F, 47·7. Calc. for K_2TiF_6: F, 47·6%).

A solution of concentration comparable to that obtained above yielded a product (II) of composition K_2TiF_6,0·95BrF_3 (Found: Br, 18·5%; equiv., 368. Calc. for K_2TiF_6,0·95BrF_3: Br, 20·5%; equiv., 370).

Samples of (I) and (II) were, without exposure to moist air, filled into Pyrex capillaries and sealed off well away from the fillings ($KBrF_4$ is thermally unstable). Photographs taken with Cu-$K\alpha$ radiation, using exposure times of 8—12 hours, showed clearly the seven strongest lines of the $KBrF_4$ powder pattern; these were the strongest lines on the photographs of (I) and (II), and the identification of $KBrF_4$ is thus beyond doubt.—University Chemical Laboratory, Cambridge. [*Received, July 24th*, 1950.]

The Purification of Brucine. By H. Kacser.

Brucine has been extensively used for resolutions and latterly for kinetical studies of mutarotation phenomena. No reliable physico-chemical assessment of purity appears to be available. In addition to pharmaceutical specifications, there are meagre and conflicting data on the specific rotation (Oudemans, *Annalen*, 1873, **166**, 69; Hilditch, *J.*, 1908, **93**, 700; Tycociner, *Rec. Trav. chim.*, 1882, **1**, 145; Jamison and Turner, *J.*, 1942, 437).

Chloroform solutions of brucine were observed to develop a pale brown colour when kept in daylight and simultaneously their optical rotatory power decreased. The processes were faster under ultraviolet irradiation. It seems likely that the process is one of photochemical oxidation since small quantities of compounds resembling closely the neutral oxidation products obtained by Leuchs and his co-workers (Leuchs and Teasmar, *Ber.*, 1937, **70**, 2369; Leuchs and Boit, *Ber.*, 1940, **73**, 885) were isolated. These compounds, together with a substance with properties similar to ϕ-brucine, could also be isolated in small quantities from samples of commercial brucine.

On account of this photo-oxidation, purification procedures such as that proposed by Saunders (*J. Amer. Chem. Soc.*, 1928, **50**, 123) which involve the liberation of moist brucine were not used in the final stages. Recrystallisation from solvents such as chloroform, carbon tetrachloride, ethanol, acetone, benzene, *p*-xylene, mesitylene, and acetophenone had disadvantages on account of retention of solvent (Kacser and Ubbelohde, *Nature*, 1949, **164**, 445) or because the solubility relationships were unfavourable. The best solvent was found to be toluene.

The course of separation was followed polarimetrically in each case. When toluene was used, the rotation of a sample of commercial brucine (B.D.H.) rose from $[\alpha]_{5461}^{20}$ = −139·6° to −149·3° (in chloroform) after one extraction and two recrystallisations and did not alter significantly on further treatment with this or other solvents.

The final procedure adopted for purification was as follows: To 10 g. of brucine (B.P.) were added 200 c.c. of toluene (sulphur-free), and the mixture was shaken vigorously for 15 minutes. The solution was filtered and then concentrated to a third of its volume at *ca.* 50° under a vacuum. The crystals which formed on cooling and shaking were filtered off, washed with a little cold toluene, and dried in a vacuum-desiccator. Subsequent recrystallisations were carried out by dissolving the base in just sufficient toluene to effect solution at 50° and cooling to room temperature.

The following constants were taken as definitive: $[\alpha]_{5461}^{20}$ = −149·5°, $[\alpha]_{5893}^{20}$ = −120·5° (*c*, 1 in pure dry chloroform). No appreciable temperature coefficient of rotation of solution was observed in the range 20—45°. A chloroform solution of purified brucine stored in blackened air-tight containers showed no significant change in rotation after 5 days.—Queen's University, Belfast. [*Received, July 24th*, 1950.]

OBITUARY NOTICES.

RONALD VICTOR GEORGE EWENS.

1913—1948.

Dr. Ronald Victor George Ewens met his death in tragic circumstances at the age of 35 on September 21st, 1948. He was educated at Queen Elizabeth's Hospital, Bristol, and went to Oxford as an Open Scholar of Lincoln College in 1932. He was a pupil of Professor N. V. Sidgwick, showed great promise as an undergraduate, and took a First Class in the Honour School of Chemistry in 1936. In the period 1936—38 he carried out an original investigation and presented a thesis entitled "The metallic carbonyls and nitrosyls." This work in which he showed great skill as an experimenter was of outstanding merit and gained for him the D.Phil. degree. For about a year after that he conducted an investigation at the Sir William Dunn School of Pathology, Oxford, into the action of snake venom in the inhibition of fermentation and glycolysis. He then joined the staff of Guy's Hospital Medical School as demonstrator in Chemistry just as the School was evacuated to Tunbridge Wells in 1939 on the outbreak of war. There he was most directly concerned with the teaching of inorganic and physical chemistry. In this he was very successful and the benefits of his wide knowledge were often sought by his colleagues in other departments. He was always generous with his time in this respect. He rendered great service to the school there and on his return to London, and later at the time of reconstruction following the war. In 1948 he had been advanced to the status of Reader.

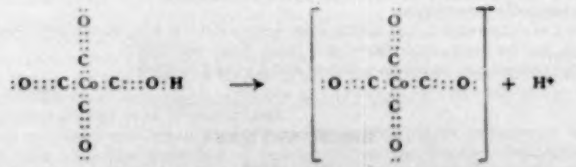
During the war further study of complex compounds of the metals was interrupted, but as soon as possible he returned to it and was energetically engaged with this and other matters. He devoted much attention to reading the MS. of N. V. Sidgwick's book on "The Chemical Elements and their Compounds," and as a result many valuable modifications were made.

Ewens's early published papers arose from his D.Phil. research. In the first of these (with L. O. Brockway and M. W. Lister) on "An Electron Diffraction Investigation of the Hexacarbonyls of Chromium, Molybdenum and Tungsten" (*Trans. Faraday Soc.*, 1938, **34**, 1351), the most probable configuration for the molecules is shown to be that of a regular octahedron and on this basis the metal–carbon distances were determined. They were found to be shorter than an expected set of distances but the shortening was not so great as that found in the carbonyls and nitrosyl carbonyls which have only four groups attached to the metal atom. The interpretation given was that resonance of the type

$$\tilde{M}-C\equiv\hat{O} \qquad\qquad M=C=O$$

gives a partial double bond character to the metal–carbon link, this effect being less marked the greater the number of bonds round the central atom.

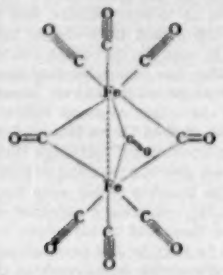
A similar investigation of iron pentacarbonyl, iron carbonyl hydride $Fe(CO)_4H_2$, and cobalt carbonyl hydride $Co(CO)_4H$ showed that the pentacarbonyl had a trigonal bipyramidal structure. For both carbonyl hydrides the CO groups are arranged tetrahedrally around the metal atom. From this it is concluded that the hydrogen atoms cannot be linked directly to the metal. The M–C–O grouping is linear and this, like the acidic character of the hydrogen atoms, is inconsistent with a $-C\lessdot^{H}_{O}$ linking. The hydrogens are therefore linked to oxygen atoms of CO groups, and the structure, *e.g.*, for the cobalt compound is



which shows its ion-forming behaviour.

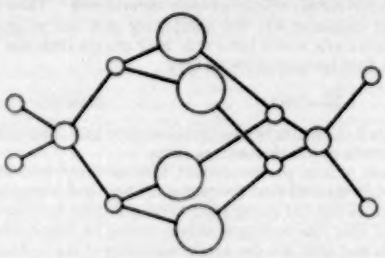
The great structural resemblance between nickel carbonyl, iron and cobalt nitrosyl carbonyls, and the carbonyl hydrides is explained. In each case the central atom has a co-ordination number four and an effective atomic number 36.

At about this time Ewens, with the writer, carried out a crystal structure examination of iron enneacarbonyl (*J.*, 1939, 286), and of this period the happiest recollections remain. Ronnie, as he was usually known, came one day into the laboratory with hard-won crystals. Unlike some who have crystals the next thing he did was to take off his coat and consequently the work started that day and was completed very quickly. It would have been done in half the time but for the demon who, as commonly happens, planted an arithmetic slip in its invariable place at the beginning of a long computation. His good-humoured comminations of that demon survive with the prolonged laugh that greeted the emergence of the molecule as



Of the several structures contemplated for this molecule, of previously unknown constitution or even molecular weight, none had been permitted anything in the nature of a $>C{=}O$ group, but three such groups, forming bridges between the two iron atoms, were found. The two iron atoms are at a distance appropriate to a covalent bond between them.

Later work by Ewens at Guy's dealt with polynuclear carbonyls and nitrosyls (*Nature*, 1948, 161, 530), and he also worked on compounds of gold and platinum. As an example, the structure suggested for tetraethylsulphatodigold $(Et_2Au)_4(SO_4)_2$ (*J.*, 1941, 109) is as shown, with



Large circles, gold; medium, sulphur; small, oxygen.

two ethyl groups attached to each gold atom. A last communication (*Nature*, 1948, 162, 693) dealt with a new method of obtaining trimethylplatinum derivatives by suitable reactions of *cis*-dipyridinotetrachloroplatinum.

This record of achievement, but for the interruptions of the war, would have been much more extensive and, had he lived, would have been many times multiplied.

In 1942 he married and he leaves a widow and a young daughter.

H. M. Powell.

ERICH HEYMANN.

1901—1949.

Physical chemistry in Australia, and particularly in the University of Melbourne, has suffered a severe loss by the death of Associate Professor Erich Heymann on November 23rd, 1949, in Chicago. He had visited England in the summer of 1949 and was travelling through the United

States of America with the aid of a Carnegie Corporation Fellowship on the return journey to Australia when he died peacefully in his sleep from coronary occlusion. His letters gave no indication of any ill-health; they reflected the enjoyment which he experienced in the rich opportunities for personal contacts and study afforded by travel and the enthusiasm with which he looked forward to resuming his own researches in Melbourne. He was unmarried and is survived in Australia by a widowed mother.

Heyman was born in Frankfurt-am-Main in 1901 and received his education in science at the universities of Munich and Frankfurt. He graduated at Frankfurt (Ph.D., *summa cum laude*) in 1924 and became research assistant at the Institute of Colloid Science in his native city, later becoming senior demonstrator and then lecturer in physical chemistry at Frankfurt University under Bonhoeffer in 1932. The increasing difficulties which beset those of Jewish origin in Germany led him to go to London, where he spent two years as I.C.I. Research Scholar under Professor F. G. Donnan. This step decided his future career, for when in 1936 an opportunity came to transfer to the University of Melbourne as Carnegie Research Scholar and lecturer in physical chemistry he accepted it on Donnan's advice. Heymann never regretted coming to Australia and spoke often in the warmest terms of the kindness and help he had received from Professor Donnan in reaching this decision. It was a source of great comfort to him when later he was able to arrange for his parents to join him in Melbourne. He became senior lecturer in 1938 and Associate Professor in Physical Chemistry in 1945. He was elected a Fellow of the Chemical Society in June, 1944.

Heymann's main interest, from his early graduate days, was in problems of colloid and surface chemistry. He was, however, both widely read and a versatile experimentalist and therefore quick to perceive and investigate important problems in other fields which were even distantly allied to his primary interest.

His earliest papers dealt with the kinetics and equilibria in the system colloidal ferric hydroxide–hydrochloric acid–water, and he showed *inter alia* that colloidal ferric hydroxide had a similar action in the hydrolysis of ferric chloride solutions to that of aluminium hydroxide in the hydrolysis of sodium aluminate.

Studies of adsorption from non-aqueous solution (with E. Boye), in which exceptions to Traube's rule were discovered, led to an investigation of the connection between the degree of adsorption and the dielectric properties of the solvent and to the study of adsorption over the complete mole-fraction range for several binary liquid mixtures. The measurement of dielectric constants gave as an interesting side investigation the determination of the dipole moment of iron pentacarbonyl. He also showed that in aqueous systems the hydrolysis of salts of noble metals was promoted by adsorption of the hydrated oxide on active carbon and that this reaction was accompanied by reduction of the oxide to the metal with the liberation of carbon dioxide, while solutions of ferric chloride were partly reduced to ferrous chloride.

A long series of investigations dealt with the properties of hydrophilic sols of proteins and methyl cellulose, the sol–gel transformation in such systems, and the interactions of the colloid with electrolytes. Such studies with methyl cellulose led naturally to an investigation of the exchange reactions between cellulose and electrolytes, and this work in turn led to the investigation of similar reactions in ion-exchange resins. The measurement of the electrical conductivity of the ions in equilibrium with the resin phase provided a convenient way of studying the binding forces involved.

Probably the most outstanding single contribution made by Heymann was the proof by the partition method that solutions of metals in their molten halides were not, as claimed by R. Lorenz and others, colloidal dispersions but true atomic solutions. This research indicated the desirability for a study of the properties of molten salt systems (ionic liquids), and he carried out with various pupils the investigation of the electrical conductivities, viscosities, surface tensions, and partial molal volumes in a number of binary systems.

Another subject which Heymann investigated was the prevention of evaporation from reservoirs by means of duplex films, a matter of great importance in the drier parts of inland Australia. Such films are remarkably effective in the laboratory but fail in the open owing mainly to the action of the wind breaking them.

Heymann's published researches occupy more than fifty papers in German, English, and American journals. He also published a monograph on the Sol–Gel Transformation. He was awarded in 1942 the Grimwade Prize for Industrial Research in Melbourne and the Smith Memorial Medal of the Royal Australian Chemical Institute "for the development of some branch of chemical science."

Heymann was an admirable teacher; his lectures were models of clarity and thoroughness,

and they were given with remarkable command of the English language, which he had learned after leaving Germany. He was a most fertile and stimulating leader in research, who was able to bring out the best qualities of his research students and co-workers through his own enthusiasm and high ideals. Combining also unfailing good humour with cheerful acceptance of responsibility and sound judgment, he was an invaluable colleague whose influence had steadily grown in the Chemistry School and in the University. His scholarly tastes, unassuming modesty of demeanour, and wide human sympathies endeared him to staff and students alike, and his sudden death while still in the prime of life has left a sense of profound loss.

I am grateful to my colleague, Mr. A. N. Hambly, for help in the preparation of this memoir.

E. J. Hartung.

GUSTAV KOMPPA.

1867—1949.

Gustav Komppa was born in Wiborg, capital of Karelia, on the 28th July, 1867. He was educated at the Wiborg Lyceum and at an early age showed his interest in scientific subjects, more especially in chemistry. Whilst at school he assisted the Science Master in the preparation of his class experiments in chemistry and physics and also took an active part in Sunday excursions for the collection of botanical and zoological specimens. Economic considerations necessitated his leaving school after only five years in the Middle School and, with the object of increasing his knowledge of chemistry, he was apprenticed to an apothecary. His duties in the pharmacy, however, left him little time for study but he was fortunate in that about a year later he was able to become a student in the Polytechnic Institute in Helsingfors. Here he pursued his studies with such diligence that in 1890 he obtained the Institute's Diploma with distinction. His first official appointment was as a chemist in the Helsingfors State Food Laboratory and this lead to the publication of his first paper entitled "The use of soda-lime as a drying agent in the Marsh test." Whilst holding this appointment he continued to work in the University and he passed the Candidate's examination in 1897. Although Komppa's interest had at first been in inorganic chemistry, yet under the influence of Professor H. A. Wahlforss, head of the Chemistry Department in the Polytechnic Institute, he gradually became interested in organic chemistry. Thus the subject for his Doctor's thesis was "Uber kernsubstituirte Styrole," the experimental work being carried out partly in the University Laboratory in Helsingfors under Professor E. Hjelt and partly at the Zurich Polytechnicum under Professor A. Hantzsch. He received the Ph.D. degree in 1894 and was in 1895 appointed Assistant Lecturer in the Polytechnic Institute, Helsingfors. Here he was to remain for his whole life, except for a short period at Leipzig in Ostwald's laboratory and a short stay in Paris. Whilst he was Assistant Lecturer, he acted as lecturer from time to time, and in 1899 he was appointed to succeed Wahlforss. On the reorganisation of the Polytechnic Institute Komppa became professor and head of the Department of Chemistry in the Finland Institute of Technology, a post which he retained until his retirement in 1937, when he became Emeritus. However, he continued his teaching and research work at the Institute until 1946. It was a crushing blow to him when his laboratory and all his specimens and notes were destroyed by an air attack in 1944.

It would be difficult to over-estimate Komppa's influence on the training of Finnish chemists and chemical engineers, which extended over a period of nearly half a century. From his students he required a high standard, and being an excellent lecturer he was able to arouse enthusiasm in even the dullest. The present chemical laboratories of the Finland Institute of Technology, completed only after his death, were with one exception designed by him.

His teaching and administrative duties were heavy, since his department was responsible not only for the teaching of inorganic, organic, and physical chemistry, but also for that in biochemistry and chemical engineering. In spite of this he found time to take a prominent part in the various scientific societies, including the Finnish Chemical Society, the Society of Finnish Chemists, and the Society of Finnish Engineers. He was the permanent secretary of the Finnish Academy of Science and Letters from 1908 to 1936, and he took a very active part in the foundation of the University of Turku, of which he was the head from 1936 to 1945. He represented Finland at many International Congresses, and Fellows of the Chemical Society will remember his last visit to this country in 1947 on the occasion of the meeting of the International Congress for Pure and Applied Chemistry.

His scientific interests were not confined to chemistry, for he was much interested in forestry and horticulture and he had an experimental plantation at Karjalohja. He published a number of papers on botanical subjects.

Komppa's services to science did not remain unrecognised. He was a member of a number of foreign academies and scientific societies. From the Finnish Government he received the Cross of Liberty, First Class, and the Grand Cross of the Order of the White Rose of Finland. He had also the Danish order of Danneborg and the Swedish order of the Polar Star.

In considering Komppa's contributions to science, of which a brief account will now be given, it should be borne in mind that practically the whole of the experimental work was carried out with his own hands. He had very few research students and it was not until 1928 that he had a paid assistant. He published about 160 memoirs which, apart from a few of minor interest, were all concerned with terpene chemistry. In 1899 (*Ber.*, **32**, 1421) he described the preparation of ββ-dimethylglutaric acid but it was not until 1901 (*Ber.*, **34**, 2472) that he published a preliminary note on the synthesis of *apo*camphoric acid, which was followed in 1903 (*Ber.*, **36**, 4332) by the classical preliminary note on the synthesis of (±)-camphoric acid. In October 1905 Komppa reported to the Finnish Chemical Society his complete synthesis of (±)-camphor, and in 1909 (*Annalen*, **370**, 209) the full account of these experiments was published, the resolution of the (±)-acid and the complete synthesis of (+)-camphor having been recorded by Beckman and Sarau in the same year (*Ber.*, **42**, 485). This was, however, only the first of the syntheses in the terpene series which we owe to Komppa, but it undoubtedly established his position as a chemist of the first rank.

Simultaneously Komppa extended his experiments with *apo*camphoric acid and he was able (*Ber.*, 1908, **41**, 2747; 1911, **44**, 863; *Annalen*, 1909, **366**, 71) to establish the structures of pinophanic acid and tricyclenecarboxylic acid; by utilising reactions similar to those used in the synthesis of camphor he converted *apo*camphoric acid into (±)-α-fenchocamphorone.

He devoted considerable attention to the chemistry of santene and its derivatives, and in a long series of memoirs (1911 to 1925) he described the synthesis of camphenilone, *iso*camphenilone, and santene, santenone, and the santenols. His most important researches, apart from camphor were, however, those relating to the fenchenes and pinene.

Mention has already been made of the synthesis of (±)-α-fenchocamphorone and this was followed later (*Ber.*, 1936, **69**, 2606) by the synthesis of (±)-β-fenchocamphorone. Other work which he carried out in this field has thrown much light on the complicated chemistry of the fenchenes, and the structures suggested by him in 1929 (*Annalen*, **470**, 129) have found general acceptance. He himself described the synthesis of α-fenchene, the partial synthesis of β- and γ-fenchenes (*Ann. Accad. Sci. Fennicae, A*, **10**, No. 3, 3), whilst in an important paper (*Annalen*, 1938, **535**, 252) he described the dehydration of the fenchyl alcohols.

It must have given him deep satisfaction when, in his last years of experimental research, he was able to record the complete synthesis of α-pinene. Already in 1937 (*Ber.*, **70**, 788) he had completed the synthesis of (±)-verbanone and (±)-δ-pinene. Five years later (*Annalen*, 1941, **547**, 185) he was able to extend this work by a brilliant synthesis of pinonic acid, pinocamphone, and α-pinene. It is given to few to leave so great a record of achievement in synthetic organic chemistry.

Komppa did not long survive the celebration of his eightieth birthday on the 28th July, 1947. Towards the end of 1948 he had a stroke, and he died on the 20th January, 1949. Komppa's wife, Siiri Andelin, by whom he had a son and a daughter, died in 1946.

J. Palmén.
J. L. Simonsen.

ROLAND VICTOR NORRIS.

1888—1950.

Dr. Roland Victor Norris died at Port Shepstone, South Africa, on the 28th April, 1950, at the age of 62. Dr. Norris went to South Africa in November, 1949, on holiday and was due to return to the Tea Research Institute of Ceylon, of which he had been Director since 1929. His death is a sad loss to the Institute he served so well, and a personal misfortune to his many friends, amongst whom may be included the whole of his Staff. After graduating from Manchester University, Dr. Norris became private assistant to Professor W. H. Perkin. Moving to the Lister Institute of Preventive Medicine, London, in 1910, he joined Professor Arthur Harden's School and took part in the classical researches on the mechanism of alcoholic

fermentation by yeast enzymes, for which work he was eventually awarded the D.Sc. degree of the London University. In 1912, during his career at " the Lister " he was elected to a Beit Memorial Fellowship.

Dr. Norris's long career in the East began in 1914 when he accepted the post of Physiological Chemist at the Imperial Bacteriological Laboratory in India. His first administrative experience was gained in the Indian Army in which his administrative abilities were soon recognised after a brief period of active service in 1915.

In 1918 onwards, Dr. Norris gradually turned towards agricultural research, first becoming Agricultural Chemist to the Government of Madras. When he was Professor of Biochemistry in the Indian Institute of Science, Bangalore, from 1924 to 1929, his research students were largely occupied with biochemical problems relating to agricultural subjects, such as soils, plants, manures, the lac industry, and the spike disease of sandalwood.

In 1929, Dr. Norris was appointed to the Directorship of the Tea Research Institute of Ceylon, when the construction of the permanent quarters at St. Coombs was just starting. The Institute has grown from its foundation on St. Coombs Estate, to its present status, under his guidance and will be a memorial to his industry so long as it exists.

" R. V." as he was known to his colleagues was by no means a pedant. He was a widely travelled and well read man of many interests. Actively interested in sports, particularly rugger and hockey, he regularly attended district games after he gave up playing himself. He enjoyed an evening at the Club as well as any planter, and took part in many social activities, especially amateur dramatics. In his later years he became keenly interest in Freemasonry and achieved the rare distinction of occupying the Chairs of two Lodges under the English Constitution and one under the Irish Constitution.

European, Indian, and Ceylonese colleagues of two generations will remember R. V. with affection. Many members of the Tea Industry will remember Roland Norris either as a personal friend or as a personality. His obituarist having worked under his direction for sixteen years may perhaps be excused a personal tribute to R. V.'s tolerant but firm direction, critical but staunch support, and his fatherly guidance and encouragement.

J. L.

Telephone: Clerkenwell 3900

Telegraphic Address: "Gasthermo, Rath, London."

B. BLACK & SON, LTD.

169, Gravrell Road, London, E.C.1.

Pilot-to-Flow Thermometers, graduated on stem, for determining hydrostatic head in Water Circulating Systems, with an accuracy of ± 1% of the total range, and within the limits specified in official Specifications. The Flow in the system is from underlay and is available to all schools with the exception of those that adopt the plan flush.

Makers of Calorimeter Thermometers, also Electrical Thermometers for Reading up all the principal Scientific Instruments and Laboratory Apparatus Manufacturers.

Annual Reports on the Progress of Chemistry

CUMULATIVE INDEX

VOL. 1 (1904) — VOL. XLVI (1949)

To be Published 1951

Price 25s. ($3.50)

The *Annual Reports* first issued by The Chemical Society in 1904 have long been recognised as containing authoritative summaries of progress in all branches of fundamental chemistry. Every significant new development during the period in question has been described and the very complete references which are provided make it possible to discover the relevant original papers on any particular topic.

A Cumulative Subject Index covering the entire series of Reports, including the volume for 1949 (published 1950), is now being prepared and will be published in the early summer of 1951.

It is considered that this Index will be of the greatest value to chemists since those in possession of a series of Annual Reports will be provided, at very moderate cost, with a most useful, yet compact, guide to the chemical literature of the period. The Index will be similar in format and binding to the *Annual Reports* and is expected to contain approximately 500 pages.

The CHEMICAL SOCIETY

BURLINGTON HOUSE · LONDON, W.1

PYREX Brand

Sintered Glassware

ensures perfect filtering

PYREX Brand Sintered Glass filters are composed entirely of PYREX Brand Glass, ground to varying degrees of fineness, and fused into PYREX Brand filtering vessels, the whole unit being resistant to the effects of sudden heat and cold.

The actual filter discs are produced in varying standards of porosity, and at present are available in five grades . . . from average pore diameter 120 microns to 1·3 microns.

PYREX Brand apparatus is therefore available for work ranging from the separation of coarse precipitates to analytical work with the finest precipitates.

PYREX Brand Scientific Glassware is supplied only through Laboratory Furnishers, but illustrated catalogue and two free copies of our Chemist's Notebook will be sent direct on application to us.

JAMES A. JOBLING & CO. LTD., Wear Glass Works, SUNDERLAND.

concentrated volumetric solutions

in ampoules for greater convenience

This new B.D.H. development has already found practical application in many laboratories. Concentrated volumetric solutions can be stored without danger of deterioration and in small space. The contents of each 2 oz. ampoule, when diluted as directed, provide 500 ml. of solution accurately standardised within the factor limits of 0.999 and 1.001.

B.D.H. CONCENTRATED VOLUMETRIC SOLUTIONS

in cartons each containing seven ampoules

further information available on request

THE BRITISH DRUG HOUSES LTD.
B.D.H. LABORATORY CHEMICALS GROUP
POOLE DORSET

Printed in Great Britain by Richard Clay and Company, Ltd., Bungay, Suffolk.